

WO03068230

Publication Title:

SUBSTITUTED PYRIDINONES AS MODULATORS OF P38 MAP KINASE

Abstract:

Courtesy of <http://worldwide.espacenet.com>

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 August 2003 (21.08.2003)

PCT

(10) International Publication Number
WO 03/068230 A1

(51) International Patent Classification⁷: **A61K 31/4412**,
A61P 29/00, C07D 213/69, 401/06, 409/06, 213/70,
213/64, 213/74, 405/06, 213/84, 401/10, 405/12, 401/12,
213/75, 401/14, 213/79, 401/04, 405/04, 413/10, 215/22,
405/14, 409/14, 213/85

(21) International Application Number: PCT/US03/04634

(22) International Filing Date: 14 February 2003 (14.02.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/357,029 14 February 2002 (14.02.2002) US
60/436,915 30 December 2002 (30.12.2002) US

(71) Applicant (for all designated States except US): **PHARMACIA CORPORATION** [US/US]; 800 Lindbergh Blvd., St. Louis, MO 63167 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DEVADAS, Balekudru** [US/US]; 2175 Parasol Drive, Chesterfield, MO 63017 (US). **WALKER, John** [US/US]; 11946 Autumn Lakes Drive, Maryland Heights, MO 63043 (US). **SELNESS, Shaun, R.** [US/US]; 1875 Cedarmill Drive, Chesterfield, MO 63017 (US). **BOEHM, Terri, L.** [US/US]; 928 Cleta Drive, Ballwin, MO 63021 (US). **DURLEY, Richard, C.** [US/US]; 509 Princeton Gate Court, Chesterfield, MO 63017 (US). **DEVRAJ, Rajesh** [IN/US]; 41 Westmead Court, Chesterfield, MO 63005 (US). **HICKORY, Brian, S.** [US/US]; 16883 Paradise Peak Circle, Wildwood, MO 63011 (US). **RUCKER, Paul, V.** [US/US]; 7487 Gannon Avenue, University City, MO 63130 (US). **JEROME, Kevin, D.** [US/US]; 2339 Pheasant Run Drive, Maryland Heights, MO 63043 (US). **MADSEN, Heather, M.** [US/US]; 746 West Canterbury Road, Apt.B, University City, MO 63132 (US). **ALVIRA, Edgardo** [US/US]; 2043 Cannon Heights Drive, Apt. 9, Chesterfield, MO

63017 (US). **PROMO, Michele, A.** [US/US]; 12445 Glenmeade Ct., Apt. J, Maryland Heights, MO 63042 (US). **BLEVIS-BAL, Radhika, M.** [US/US]; 2153 Oak Drive, St. Louis, MO 63131 (US). **MARRUFO, Laura, D.** [US/US]; 5 Sunny Forest Court, Ellisville, MO 63011 (US). **HITCHCOCK, Jeff** [US/US]; 524 Foxbriar Drive, Saint Peters, MO 63376 (US). **OWEN, Thomas** [US/US]; 1774 Canyon View Court, Chesterfield, MO 63017 (US). **NAING, Win** [MM/US]; 1198 Noonng Tree Drive, Chesterfield, MO 63017 (US). **XING, Li** [CN/US]; 15739 Tambour Court, Chesterfield, MO 63017 (US). **SHIEH, Huey, S.** [US/US]; 13120 Amiot Court, St. Louis, MO 63146 (US). **SAMBANDAM, Aruna** [IN/US]; 84-C Yorkshire Drive, Guilderland, NY 12084 (US). **LIU, Shuang** [CN/US]; 302 Polsinelli Drive, Schenectady, NY 12303 (US). **SCOTT, Ian, L.** [GB/US]; 15312 162nd Avenue NE, Woodinville, WA 98072 (US). **MCGEE, Kevin, F.** [US/US]; 20B Brookedge, Guilderland, NY 12084 (US).

(74) Agent: **SARUSSI, Steven, J.**; McDonnell Boehnen Hulbert & Berghoff, Suite 3200, 300 South Wacker Drive, Chicago, IL 60606 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

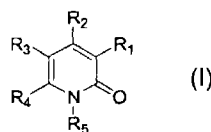
(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

[Continued on next page]

(54) Title: SUBSTITUTED PYRIDINONES AS MODULATORS OF P38 MAP KINASE



(57) Abstract: Disclosed are compounds of Formula (I) and pharmaceutically acceptable salts thereof, wherein R₁, R₂, R₃, R₄, and R₅ are defined herein. These compounds are useful for treating diseases and conditions caused or exacerbated by unregulated p38 MAP Kinase and/or TNF activity. Pharmaceutical compositions containing the compounds, methods of preparing the compounds and methods of treatment using the compounds are also disclosed.



— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

SUBSTITUTED PYRIDINONES AS MODULATORS OF P38 MAP KINASECross Reference to Related Applications

This application claims priority from U.S. Provisional Application Serial Number 60/357,029, filed February 14, 2002, and U.S. Provisional Application Serial Number 60/436,915, filed December 30, 2002, the disclosure of each of which is incorporated herein by reference in its entirety.

Background of the invention10 Field of the invention

The instant invention relates to substituted pyridinones that are useful for treating diseases and conditions caused or exacerbated by unregulated p38 MAP kinase activity.

Pharmaceutical compositions containing the pyridinone compounds, methods of preparing the pyridone compounds and methods of treatment using the compounds are also disclosed.

Description of the Related Art

Numerous cell surface receptors use one or more of the mitogen-activated protein kinase (MAP kinase) cascades during signal transduction. MAP kinases are a family of protein-directed serine/threonine kinases that are activated by dual phosphorylation. One subgroup of the MAP kinases is p38 MAP kinase, which is activated by a variety of signals including proinflammatory cytokines such as tumor necrosis factor (TNF) and interleukin-1 (IL-1), as well as bacterial lipopolysaccharides and environmental stress such as osmotic shock and ultraviolet radiation (Ono, K. and J. Han, Cell Signal. 12: 1, 2000). Within the p38 kinase family, there are four distinct isozymes: p38 alpha, p38 beta, p38 gamma, and p38 delta. The p38 kinase family function downstream of an activating stimulus by phosphorylating and activating transcription factors (e.g. ATF2, CHOP and MEF2C) as well as

other kinases (e.g. MAPKAP-2 and MAPKAP-3) (Trends in Cell biology 7, 353-361, 1997; Mol Cell Biology 19, 21-30, 1999; EMBO J 20, 466-479, 2001). Upon activation, the p38 kinase cascade leads to the induction of gene expression of several factors involved in inflammation and immunity including TNF, interleukin-6, granulocyte-macrophage colony stimulating factor (GM-CSF), and HIV long terminal repeat (Paul et al., Cell Signal. 9: 403-410, 1997). The products of the p38 phosphorylation stimulate the production of inflammatory cytokines and other proteins, including TNF and IL-1, and cyclooxygenase-2, and also possibly modulate the effects of these cytokines on their target cells, and thus stimulate inflammation processes (Lee, J.C. et al, Nature, 372: 376, 1994).

P38 MAP kinases have also been shown to promote apoptosis during ischemia in cardiac myocytes, which suggests that p38 MAP kinase inhibitors can be used to treat ischemic heart disease (J. Biol. Chem. 274, 6272, 1999). They are also required for T-cell HIV-1 replication and may be useful targets for AIDS therapy. P38 pathway inhibitors have been used to increase cancer cell sensitivity to cancer therapy also find use in the treatment of asthma (JPET 293, 281, 2000).

TNF is a cytokine and a potent proinflammatory mediator implicated in inflammatory conditions such as arthritis, asthma, septic shock, non-insulin dependent diabetes mellitus, multiple sclerosis, asthma, and inflammatory bowel disease. Thus inhibitors of p38 MAP kinases (required for TNF production) may be useful for the treatment of inflammatory conditions resulting from excessive cytokine production such as arthritis. (Boehm, J.C. and J.L. Adams, Exp. Opin. Ther. Patents 10: 25, 2000, and references cited therein). TNF has also been implicated in viral infections, such as HIV,

influenza virus, and herpes virus including herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, human herpesvirus-6 (HHV-6), human herpesvirus-7
5 (HHV-7), human herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis, among others.

Excessive or unregulated TNF production has also been shown to produce elevated levels of IL-1. Inhibition of TNF, therefore, should reduce levels of IL-1 (European Cytokine
10 Netw 6, 225, 1995) and ameliorate disease states caused by unregulated IL-1 synthesis. Such disease states include rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, sepsis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, adult respiratory
15 distress syndrome, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, bone resorption diseases, reperfusion injury, graft versus host reaction, alallograft rejections, fever and myalgias due to infection, cachexia secondary to infection or malignancy,
20 cachexia secondary to acquired immune deficiency syndrome (AIDS), AIDS related complex (ARC), keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis, and pyresis.

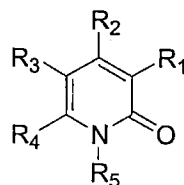
IL-1 has also been shown to mediate a variety of
25 biological activities such as the activation of T-helper cells, induction of fever, stimulation of prostaglandin or collagenase production, neutrophil chemotaxis, and the suppression of plasma iron levels (Rev. Infect. Disease, 6, 51 (1984)). Elevated levels of IL-1 have also been implicated in
30 mediating or exacerbating a number of disease states including rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease,

ulcerative colitis, anaphylaxis, muscle degeneration, cachexia, Reiter's syndrome, type I and type II diabetes, bone resorption diseases, ischemia reperfusion injury, arteriosclerosis, brain trauma, multiple sclerosis, sepsis, 5 septic shock, and toxic shock syndrome. Viruses sensitive to TNF inhibition, such as HIV-1, HIV-2, HIV-3, are also affected by IL-1 production. In rheumatoid arthritis, both IL-1 and TNF induce collagenase synthesis and ultimately lead to tissue destruction within arthritic joints (*Lymphokine Cytokine Res.* 10 (11): 253-256, (1992) and *Clin. Exp. Immunol.* 989:244-250, (1992)).

IL-6 is another pro-inflammatory cytokine, which is associated with many conditions including inflammation. Consequently, TNF, IL-1 and IL-6 affect a wide variety of 15 cells and tissues and are important inflammatory mediators of a wide variety of disease states and conditions. The inhibition of these cytokines by inhibition or modulation of p38 kinase is of benefit in controlling, reducing and alleviating many of these disease states and conditions. 20 Therefore, the present invention concerns finding small molecule inhibitors or modulators of p38 kinase and the p38 kinase pathway.

Summary of the Invention

In a broad aspect, the invention provides compounds of Formula I (Embodiment I):



(I)

and pharmaceutically acceptable salts thereof, wherein

R₁ is H, halogen, NO₂, alkyl, carboxaldehyde, hydroxyalkyl, dihydroxyalkyl, arylalkoxy, arylalkyl, alkenyl, alkynyl, arylalkynyl, -CN, aryl, alkanoyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkoxy, carboxyl, or arylalkanoyl,

wherein the aryl portion of arylalkoxy, arylalkyl, and arylalkanoyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, haloalkyl, haloalkoxy or CO₂R;

wherein the alkyl portion of the alkyl, hydroxyalkyl, dihydroxyalkyl, arylalkoxy, arylalkyl, alkanoyl, alkoxy, alkoxyalkyl and arylalkanoyl groups is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkoxy, C₁-C₄ alkoxycarbonyl, or C₃-C₇ cycloalkyl;

R₂ is H, OH, halogen, -OSO₂-(C₁-C₆) alkyl, -OSO₂-aryl, arylalkoxy, aryloxy, arylthio, arylthioalkoxy, arylalkynyl, alkoxy, aryloxy(C₁-C₆)alkyl, alkyl, alkynyl, -OC(O)NH(CH₂)_naryl, -OC(O)N(alkyl)(CH₂)_naryl, alkoxyalkoxy, dialkylamino, alkyl, alkoxy, aryl, arylalkyl, heteroaryl, heteroarylalkyl, arylalkenyl, heterocycloalkyl, heterocycloalkylalkyl, alkoxyalkoxy, NR₈R₉, dialkylamino, or CO₂R, wherein

n is 0, 1, 2, 3, 4, 5 or 6;

each of which groups is unsubstituted or substituted with
 1, 2, 3, 4, or 5 groups that are independently
 halogen, $-(C_1-C_6)alkyl-N(R)-CO_2R_{30}$, haloalkyl,
 heteroaryl, heteroarylalkyl, $-NR_6R_7$, $R_6R_7N-(C_1-C_6$
 5 $alkyl)-$, $-C(O)NR_6R_7$, $-(C_1-C_4)alkyl-C(O)NR_6R_7$, $-(C_1-C_4$
 $alkyl)-NRC(O)NR_{16}R_{17}$, haloalkoxy, alkyl, CN,
 hydroxyalkyl, dihydroxyalkyl, alkoxy,
 alkoxycarbonyl, phenyl, $-SO_2$ -phenyl wherein the
 phenyl and $-SO_2$ -phenyl groups are optionally
 10 substituted with 1, 2, or 3 groups that are
 independently halogen or NO_2 , or $-OC(O)NR_6R_7$, wherein
 R_{16} and R_{17} are independently H or C_1-C_6 alkyl; or
 R_{16} , R_{17} and the nitrogen to which they are attached
 form a morpholinyl ring;
 15 R_6 and R_7 are independently at each occurrence H,
 alkyl, hydroxyalkyl, dihydroxyalkyl, alkoxy,
 alkanoyl, arylalkyl, arylalkoxy,
 alkoxycarbonyl, $-SO_2$ -alkyl, OH, alkoxy,
 alkoxyalkyl, arylalkoxycarbonyl, $-(C_1-C_4)alkyl-$
 20 CO_2 -alkyl, heteroarylalkyl, or arylalkanoyl,
 wherein each is unsubstituted or substituted
 with 1, 2, or 3 groups that are independently,
 halogen, OH, SH, heterocycloalkyl,
 heterocycloalkylalkyl, C_3-C_7 cycloalkyl, alkoxy,
 25 NH_2 , $NH(alkyl)$, $N(alkyl)(alkyl)$, $-O$ -alkanoyl,
 alkyl, haloalkyl, carboxaldehyde, or
 haloalkoxy; or
 R_6 , R_7 , and the nitrogen to which they are attached
 form a morpholinyl, pyrrolidinyl,
 30 thiomorpholinyl, thiomorpholinyl S-oxide,
 thiomorpholinyl S,S-dioxide, piperidinyl,
 pyrrolidinyl, or piperazinyl ring which is
 optionally substituted with 1 or 2 groups that

are independently C₁-C₄ alkyl, alkoxy, carbonyl, C₁-C₄ alkoxy, hydroxyl, hydroxyalkyl, dihydroxyalkyl, or halogen;

R at each occurrence is independently hydrogen or C₁-C₆ alkyl optionally substituted with 1 or 2 groups that are independently OH, SH, halogen, amino, monoalkylamino, dialkylamino or C₃-C₆ cycloalkyl;

R₃₀ is C₁-C₆ alkyl optionally substituted with 1 or 2 groups that are independently OH, SH, halogen, amino, monoalkylamino, dialkylamino or C₃-C₆ cycloalkyl;

each R₈ is independently hydrogen, alkyl, alkanoyl, arylalkyl and arylalkanoyl, wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, alkoxy, alkoxy, carbonyl, halogen, or haloalkyl;

each R₉ is hydrogen, alkyl, alkanoyl, arylalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, heteroaryl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, arylalkanoyl, -SO₂-phenyl, and aryl wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, alkoxy, alkoxy, carbonyl, halogen, or haloalkyl;

R₃ is H, halogen, alkoxy, carbonyl, arylalkoxy, carbonyl, aryloxy, carbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl, arylalkoxy, -OC(O)N(alkyl)(CH₂)_naryl, aryloxy, arylthio, thioalkoxy, arylthioalkoxy, alkenyl, -NR₆R₇, NR₆R₇-(C₁-C₆)alkyl, or alkyl, wherein

the aryl portion of arylalkoxy, carbonyl, aryloxy, carbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl, arylalkoxy, -OC(O)N(alkyl)(CH₂)_naryl, and arylthioalkoxy, is

unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently, halogen, alkoxy, alkyl, haloalkyl, or haloalkoxy, wherein n is 0, 1, 2, 3, 4, 5, or 6; or

5 R₄ is hydrogen or R₄ is alkyl unsubstituted or substituted with
one or two groups that are independently CO₂R, -CO₂-(C₁-
C₆)alkyl, -C(O)NR₆R₇, -C(O)R₆, -N(R₃₀)C(O)NR₁₆R₁₇, -
N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, arylalkoxy, arylalkyl,
heteroaryl, heteroarylalkyl, hydroxyalkyl,
10 dihydroxyalkyl, haloalkyl, R₆R₇N-(C₁-C₆ alkyl)-, -NR₆R₇,
alkoxy, carboxaldehyde, -C(O)NR₆R₇, CO₂R, alkoxyalkyl, or
alkoxyalkoxy, wherein the heteroaryl or aryl portions of
is the above are unsubstituted or substituted with 1, 2,
3, 4, or 5 groups that are independently halogen,
15 hydroxy, alkoxy, alkyl, -CO₂-(C₁-C₆)alkyl, -CONR₆R₇, -NR₆R₇,
R₆R₇N-(C₁-C₆)alkyl-, nitro, haloalkyl, or haloalkoxy; and
R₅ is H, aryl, arylalkyl, arylthioalkyl, alkyl optionally
substituted with 1, 2, or 3 groups that are independently
arylalkoxycarbonyl, -NR₈R₉, halogen, -C(O)NR₈R₉,
20 alkoxycarbonyl, C₃-C₇ cycloalkyl, or alkanoyl, alkoxy,
alkoxyalkyl optionally substituted with one
trimethylsilyl group, amino, alkoxycarbonyl,
hydroxyalkyl, dihydroxyalkyl, alkynyl, -SO₂-alkyl, alkoxy
optionally substituted with one trimethylsilyl group,
25 heterocycloalkylalkyl, cycloalkyl, cycloalkylalkyl, -
alkyl-S-aryl, -alkyl-SO₂-aryl, heteroarylalkyl,
heterocycloalkyl, heteroaryl, or alkenyl optionally
substituted with alkoxycarbonyl, wherein
each of the above is unsubstituted or substituted with 1,
30 2, 3, 4, or 5 groups that are independently alkyl,
halogen, alkoxy, hydroxyalkyl, dihydroxyalkyl,
arylalkoxy, thioalkoxy, alkoxycarbonyl,
arylalkoxycarbonyl, CO₂R, CN, OH, hydroxyalkyl

dihydroxyalkyl, amidinooxime, $-NR_6R_7$, $-NR_8R_9$, R_6R_7N-
(C_1-C_6 alkyl)-, carboxaldehyde, SO_2 alkyl, $-SO_2H$, $-$
 $SO_2NR_6R_7$, alkanoyl wherein the alkyl portion is
optionally substituted with OH, halogen or alkoxy, $-$
5 $C(O)NR_6R_7$, $-(C_1-C_4$ alkyl)- $C(O)NR_6R_7$, amidino,
haloalkyl, $-(C_1-C_4$ alkyl)- $NR_{15}C(O)NR_{16}R_{17}$, $-(C_1-C_4$
alkyl)- $NR_{15}C(O)R_{18}$, $-O-CH_2-O$, $-O-CH_2CH_2-O-$, or
haloalkoxy; wherein

R_{15} is H or C_1-C_6 alkyl; and

10 R_{18} is C_1-C_6 alkyl optionally substituted with $-O-(C_2-C_6$
alkanoyl, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl,
 C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl; amino C_1-C_6
alkyl, mono or dialkylamino C_1-C_6 alkyl.

The invention also includes the intermediates that are
15 useful in making the compounds of the invention.

These compounds bind and/or interact with p38 kinase
and/or TNF. Preferably, they inhibit the activity of p38
kinase and/or TNF. They are therefore used in treating p38
map kinase or TNF mediated disorders. Preferably they are
20 used in treating p38 alpha or TNF mediated disorders.

The instant invention also includes pharmaceutical
compositions comprising at least one compound of formula I and
at least one pharmaceutically acceptable carrier, solvent,
adjuvant or excipient.

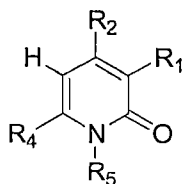
25 The instant invention also includes methods of treating a
TNF mediated disorder, a p38 kinase mediated disorder,
inflammation and/or arthritis in a subject, the method
comprising treating a subject having or susceptible to such
disorder or condition with a therapeutically-effective amount
30 of a compound of Formula I.

Detailed Description of the Invention

In a preferred aspect, the invention provides compounds of formula I wherein:

- 5 when R_2 is benzyloxy, R_3 is H, R_4 is H, and R_5 is benzyl or methyl, R_1 is not hydrogen;
 no more than two of R_1 , R_2 , R_4 , and R_5 are simultaneously hydrogen;
 R_6 and R_7 are not simultaneously OH;
 10 when R_2 is OH, R_4 is methyl and R_5 is phenyl, R_1 is not acetyl;
 and
 R_4 and R_5 are not simultaneously hydrogen.

Embodiment 2. Compounds of the formula:



- 15 and the pharmaceutically acceptable salts thereof, wherein
 R_1 is H, halogen, alkyl, carboxaldehyde, hydroxyalkyl, dihydroxyalkyl, arylalkoxy, arylalkyl, alkenyl, alkynyl, arylalkynyl, CN, alkanoyl, alkoxy, alkoxyalkyl, haloalkyl, carboxyl, or arylalkanoyl,
 20 wherein the aryl portion of arylalkoxy, arylalkyl, and arylalkanoyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, nitro, CN, haloalkyl, haloalkoxy or CO_2R ;
 25 wherein the alkyl portion of the alkyl, hydroxyalkyl, dihydroxyalkyl, arylalkoxy, arylalkyl, alkanoyl, alkoxy, alkoxyalkyl and arylalkanoyl groups is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1 - C_4 alkoxy, C_1 - C_4
 30 alkoxycarbonyl, or cyclopropyl;

R₂ is H, OH, halogen, -OSO₂-(C₁-C₆) alkyl, -OSO₂-aryl, arylalkoxy, aryloxy, arylthioalkoxy, arylalkynyl, alkoxy, phenyloxy(C₁-C₆)alkyl, -OC(O)NH(CH₂)_naryl, -OC(O)N(alkyl)(CH₂)_naryl, alkyl, alkynyl, alkoxyalkoxy, dialkylamino, heteroaryl, heterocycloalkyl, aryloxyalkyl, or CO₂R, wherein

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -NR₆R₇, haloalkyl, haloalkoxy, alkyl, heteroaryl, heteroarylalkyl, -(C₁-C₄)alkyl-C(O)NR₆R₇, R₆R₇N-(C₁-C₆alkyl)-, -C(O)NR₆R₇, -(C₁-C₄alkyl)-NRC(O)NR₁₆R₁₇, CN, hydroxyalkyl, dihydroxyalkyl, -OC(O)NR₆R₇, or -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, wherein

R₁₆ and R₁₇ are independently H or C₁-C₆ alkyl; or

R₁₆, R₁₇ and the nitrogen to which they are attached form a morpholinyl ring;

R₆ and R₇ are independently at each occurrence H, alkyl, hydroxyalkyl, dihydroxyalkyl, alkoxy, alkoxyalkyl, alkanoyl, arylalkyl, arylalkoxy, arylalkoxycarbonyl, or arylalkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, alkyl, OH, SH, carboxaldehyde, haloalkyl, or haloalkoxy; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, dihydroxyalkyl, or halogen;

n is 0, 1, 2, 3, 4, 5 or 6;

R at each occurrence is independently H or C₁-C₆ alkyl optionally substituted with 1 or 2 groups that are independently OH, SH, halogen, amino, monoalkylamino, dialkylamino or C₃-C₆ cycloalkyl;

R₃₀ is C₁-C₆ alkyl optionally substituted with 1 or 2 groups that are independently OH, SH, halogen, amino, monoalkylamino, dialkylamino or C₃-C₆ cycloalkyl;

10 R₄ is H, alkyl optionally substituted with one or two groups that are independently CO₂R, -CO₂alkyl, -C(O)NR₆R₇, -C(O)R₆, -N(R₃₀)C(O)NR₁₆R₁₇, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, arylalkoxy, heteroaryl, arylalkyl, hydroxyalkyl, dihydroxyalkyl, haloalkyl, -NR₆R₇, -C(O)NR₆R₇, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein
15 the heteroaryl or aryl portions of the above are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, hydroxy, alkoxy, alkyl, -CO₂-(C₁-C₆)alkyl, -CONR₆R₇, -NR₆R₇,
20 R₆R₇N-(C₁-C₆)alkyl-, nitro, haloalkyl, or haloalkoxy; and

R₅ is H, arylalkyl, alkyl optionally substituted with 1, 2, or 3 groups that are independently arylalkoxycarbonyl, -NR₈R₉, halogen, -C(O)NR₈R₉, alkoxycarbonyl, or alkanoyl, alkoxyalkyl optionally substituted with one trimethylsilyl group, alkoxycarbonyl, amino, hydroxyalkyl, dihydroxyalkyl, alkenyl optionally substituted with alkoxycarbonyl, alkynyl, -SO₂-alkyl, aryl, alkoxy optionally substituted with one trimethylsilyl group, heterocycloalkylalkyl, heteroarylalkyl, heterocycloalkyl, or heteroaryl, wherein
30 each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl,

halogen, alkoxy, arylalkoxy, hydroxyalkyl,
 dihydroxyalkyl, thioalkoxy, -SO₂alkyl,
 alkoxycarbonyl, arylalkoxycarbonyl, CO₂R, CN, OH,
 amidinooxime, NR₈R₉, R₆R₇N-(C₁-C₆ alkyl)-, -C(O)NR₆R₇,
 5 amidino, hydroxyalkyl, dihydroxyalkyl,
 carboxaldehyde, -NR₆R₇, haloalkyl, -(C₁-C₄ alkyl)-
 C(O)NR₆R₇, -(C₁-C₄ alkyl)-CO₂R, -(C₁-C₄ alkyl)-C₁-C₆
 alkoxycarbonyl, -(C₁-C₄ alkyl)-CN, -(C₁-C₄ alkyl)-
 NR₁₅C(O)R₁₈, -O-CH₂-O-, -O-CH₂CH₂-O-, phenyl or
 10 haloalkoxy;
 R₈ is hydrogen, alkyl, alkanoyl, arylalkyl and
 arylalkanoyl;
 R₉ is alkyl, alkanoyl, arylalkyl, heteroaryl,
 aminoalkyl, monoalkylaminoalkyl,
 15 dialkylaminoalkyl, and arylalkanoyl.

Embodiment 3. Compounds according to embodiment 2
 wherein

R₁ is H, halogen, alkyl optionally substituted with C₁-C₄
 20 alkoxycarbonyl, carboxaldehyde, hydroxyalkyl,
 dihydroxyalkyl, phenyl(C₁-C₆)alkoxy, phenyl(C₁-C₆)alkyl,
 CN, alkanoyl, alkoxy, C₂-C₄ alkynyl, C₂-C₆ alkenyl
 optionally substituted with C₁-C₄ alkoxycarbonyl,
 alkoxyalkyl, haloalkyl, or phenyl(C₁-C₆)alkanoyl,
 25 wherein the phenyl groups are unsubstituted or
 substituted with 1, 2, 3, 4, or 5 groups that are
 independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy,
 nitro, CN, CF₃, OCF₃ or CO₂R;

wherein the alkyl groups are unsubstituted or substituted
 30 with 1, 2, or 3 groups that are independently halogen,
 methoxy, or ethoxy;

R₂ is OH, phenyl(C₁-C₆)alkoxy, phenyloxy, phenyloxy(C₁-C₆)alkyl,
 phenyl(C₁-C₄)thioalkoxy, C₁-C₈ alkoxy, alkoxyalkoxy, -O-

SO₂phenyl, alkynyl, phenyl (C₂-C₄) alkynyl, alkyl,
 -OC(O)NH(CH₂)_nphenyl, -OC(O)N(alkyl)(CH₂)_nphenyl,
 dialkylamino, pyridyl, pyrimidyl, pyridazyl, pyrazolyl,
 imidazolyl, pyrrolyl, tetrahydroquinolinyl,
 5 tetrahydroisoquinolinyl, tetrazolyl, pyrazinyl,
 benzimidazolyl, triazinyl, tetrahydrofuryl, piperidinyl,
 hexahydropyrimidinyl, thiazolyl, thienyl, or CO₂R, wherein
 n is 0, 1, 2, 3, 4, 5 or 6;

each of the above is unsubstituted or substituted with 1,
 10 2, 3, 4, or 5 groups that are independently halogen,
 NR₆R₇, haloalkyl, haloalkoxy, hydroxyalkyl,
 dihydroxyalkyl, alkyl, phenyl, pyridyl, piperidinyl,
 piperazinyl, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, R₆R₇N-(C₁-C₆
 alkyl)-, -C(O)NR₆R₇, -(C₁-C₄)alkyl-C(O)NR₆R₇, -(C₁-C₄
 15 alkyl)-NRC(O)NR₁₆R₁₇, or -OC(O)NR₆R₇, wherein

R₆ and R₇ are independently at each occurrence H,
 alkyl, (C₁-C₄) hydroxyalkyl, (C₁-C₄)
 dihydroxyalkyl, (C₁-C₄) alkoxy, (C₁-C₄) alkoxy
 (C₁-C₄) alkyl, (C₁-C₄) alkanoyl, phenyl (C₁-C₄)
 20 alkyl, phenyl (C₁-C₄) alkoxy, phenyl (C₁-C₄)
 alkoxycarbonyl, or phenyl (C₁-C₄) alkanoyl,
 wherein each of the above is unsubstituted or
 substituted with 1, 2, or 3 groups that are
 independently, halogen, OH, SH, C₃-C₆
 25 cycloalkyl, (C₁-C₄) alkoxy, (C₁-C₄) alkyl, CF₃,
 carboxaldehyde, NH₂, NH(C₁-C₆)alkyl, N(C₁-
 C₆)alkyl (C₁-C₆)alkyl, OCF₃; or

R₆, R₇, and the nitrogen to which they are attached
 form a morpholinyl, thiomorpholinyl,
 30 piperidinyl, pyrrolidinyl, or piperazinyl ring
 which is optionally substituted with 1 or 2
 groups that are independently C₁-C₄ alkyl,
 hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄

dihydroxyalkyl, C₁-C₄ alkoxy carbonyl, or halogen; and

R₄ is H, alkyl optionally substituted with one or two groups that are independently CO₂R, -CO₂alkyl, -C(O)NR₆R₇,
 5 -C(O)R₆, -N(R₃₀)C(O)NR₁₆R₁₇, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, -C(O)NR₆R₇, phenyl(C₁-C₆)alkoxy, phenyl(C₁-C₆)alkyl, hydroxyalkyl, dihydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein

the phenyl groups are unsubstituted or substituted with

10 1, 2, 3, 4, or 5 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, CF₃, OCF₃;

R₅ is phenyl(C₁-C₆)alkyl, (C₁-C₆)alkyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently phenyl C₁-C₄ alkoxy carbonyl, -NR₈R₉, halogen, -C(O)NR₈R₉,
 15 alkoxy carbonyl, or alkanoyl, phenyl, alkoxy, C₂-C₆ alkynyl, C₂-C₆ alkenyl optionally substituted with alkoxy carbonyl, indolyl, quinoliny, isoquinoliny, isoindolyl, dihydroindolyl, pyrazolyl, imidazolyl, dihydroisoindolyl, indolon-2-yl, indazolyl,
 20 benzimidazolyl, pyridyl, imidazolidine dione, pyrazolyl(C₁-C₆ alkyl), imidazolyl(C₁-C₆ alkyl), piperidiny(C₁-C₆)alkyl, pyrrolidiny(C₁-C₆)alkyl, imidazolidiny(C₁-C₆)alkyl, tetrahydroisoquinoliny(C₁-C₆)alkyl, 1H-indazolyl(C₁-C₆)alkyl, dihydroindolon-2-yl(C₁-C₆ alkyl),
 25 indoliny(C₁-C₆ alkyl), dihydrobenzimidazolyl(C₁-C₆ alkyl), or dihydrobenzoimidazolonyl(C₁-C₆ alkyl), pyridyl(C₁-C₆)alkyl, pyridaziny(C₁-C₆)alkyl, pyrimidiny(C₁-C₆)alkyl, pyraziny(C₁-C₆)alkyl, tetrahydrofuryl(C₁-C₆)alkyl,
 30 naphthyl(C₁-C₆)alkyl, morpholiny(C₁-C₆)alkyl, tetrahydrofuryl(C₁-C₆)alkyl, thienyl(C₁-C₆)alkyl, piperaziny(C₁-C₆)alkyl, indolyl(C₁-C₆)alkyl, quinoliny(C₁-C₆)alkyl, isoquinoliny(C₁-C₆)alkyl,

isoindolyl(C₁-C₆) alkyl, dihydroindolyl(C₁-C₆) alkyl,
 pyrazolyl(C₁-C₄) alkyl, imidazolyl(C₁-C₄) alkyl,
 dihydroisoindolyl(C₁-C₆) alkyl, indoon-2-yl(C₁-C₆) alkyl,
 indolon-2-yl(C₁-C₆) alkyl, or morpholinyl C₁-C₆ alkyl,

5

wherein

each of the above is unsubstituted or substituted with 1,
 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl,
 halogen, C₁-C₆ alkoxy, phenyl C₁-C₆ alkoxy, C₁-C₆
 thioalkoxy, C₁-C₆ alkoxycarbonyl, CO₂R, CN, -SO₂(C₁-
 10 C₆)alkyl, amidinooxime, NR₈R₉, -NR₆R₇, NR₆R₇ C₁-C₆ alkyl,
 -C(O)NR₆R₇, -(C₁-C₄)alkyl-C(O)NR₆R₇, amidino, C₁-C₄
 haloalkyl, hydroxy C₁-C₆ alkyl, C₁-C₆ dihydroxyalkyl, or
 C₁-C₄ haloalkoxy; wherein

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl
 15 C₁-C₆ alkyl and phenyl C₁-C₆ alkanoyl; and

R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl,
 di C₁-C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-
 C₆ alkanoyl, phenyl C₁-C₆ alkyl, indazolyl, and
 phenyl C₁-C₆ alkanoyl.

20

Embodiment 4. Compounds according to embodiment 3,
 wherein

R₁ is H, halogen, C₁-C₄ alkyl optionally substituted with C₁-C₄
 alkoxycarbonyl, C₂-C₄ alkenyl optionally substituted with
 25 C₁-C₄ alkoxycarbonyl, C₂-C₄ alkynyl, or carboxaldehyde;

R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, phenyl
 (C₁-C₄) thioalkoxy, or pyridyl; wherein each of the above
 is optionally substituted with 1, 2, 3, 4, or 5 groups
 that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀,
 30 NR₆R₇, -(C₁-C₄)alkyl-C(O)NR₆R₇, (C₁-C₄) haloalkyl,
 -C(O)NR₆R₇, -(C₁-C₄ alkyl)-NRC(O)NR₁₆R₁₇, (C₁-C₄) haloalkoxy,
 hydroxyalkyl, C₁-C₆ dihydroxyalkyl, (C₁-C₆) alkyl, pyridyl,
 or R₆R₇N-(C₁-C₆ alkyl)-.

Embodiment 4a. Compounds according to embodiment 4, wherein R₁ is H.

5 Embodiment 4b. Compounds according to embodiment 4, wherein R₁ is halogen.

Embodiment 4c. Compounds according to embodiment 4, wherein R₁ is C₁-C₄ alkyl optionally substituted with C₁-C₄ alkoxy carbonyl.

10

Embodiment 5. Compounds according to embodiment 4, wherein R₅ is indolyl, pyridyl, pyridazinyl, pyrimidinyl, indazolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, pyrazolyl, imidazolyl, furanyl, quinolinyl, isoquinolinyl, isoindolyl, dihydroindolyl, dihydroisoindolyl, indolon-2-yl, or pyrazinyl, each of which is unsubstituted or substituted with 1, 2, 3, 4 or 5 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, dihydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -NR₆R₇, -(C₁-C₄)alkyl-C(O)NR₆R₇, -NR₈R₉, NR₆R₇-(C₁-C₄ alkyl), -C(O)NR₆R₇, or amidinoxime; wherein R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl C₁-C₄ alkyl, phenyl C₁-C₄ alkoxy, or phenyl C₁-C₄ alkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, SH, C₃-C₆ cycloalkyl, aryl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃; or R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄

30

alkyl, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 6. Compounds according to embodiment 5,

5 wherein

R₅ is indolyl, pyridyl, pyrimidinyl, pyrazolyl, furanyl, indazolyl, dihydroindolyl, dihydroisoindolyl, indolon-2-yl, or pyrazinyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups that are
10 independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -C(O)NR₆R₇, -NR₈R₉, -(C₁-C₄)alkyl-C(O)NR₆R₇, -NR₆R₇, NR₆R₇-(C₁-C₄ alkyl)-, and amidinooxime.

15

Embodiment 7. Compounds according to embodiment 6,

wherein

R₅ is indolyl, pyridyl, pyrimidinyl, dihydroindolyl, dihydroisoindolyl, pyrazolyl, or pyrazinyl, each of which
20 is unsubstituted or substituted with 1, 2, 3, or 4 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -C(O)NR₆R₇, NR₈R₉, -(C₁-C₄)alkyl-C(O)NR₆R₇, -NR₆R₇, NR₆R₇-(C₁-C₄ alkyl)-, or
25 amidinooxime; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkanoyl, C₁-C₄ alkoxy C₁-C₄ alkyl, each of which is optionally substituted with 1, 2, or 3
30 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

Embodiment 8. Compounds according to embodiment 7,
wherein

R₅ is indolyl, pyridyl, pyrimidinyl, dihydroindolyl,
dihydroisoindolyl, pyrazolyl, or pyrazinyl, each of which
5 is unsubstituted or substituted with 1, 2, or 3 groups
that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, C₁-
C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkoxy,
-C(O)NR₆R₇, -(C₁-C₄)alkyl-C(O)NR₆R₇, NR₈R₉, -NR₆R₇, or NR₆R₇-
(C₁-C₄ alkyl)-; wherein

10 R₆ and R₇ are independently at each occurrence H, C₁-C₄
alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄
alkanoyl, or C₁-C₄ alkoxy, each of which is
optionally substituted with 1, 2, or 3 groups that
are independently halogen, OH, SH, C₃-C₆ cycloalkyl,
15 C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

Embodiment 9. Compounds according to embodiment 4,
wherein

R₅ is phenyl, phenyl(C₁-C₆)alkyl, or (C₁-C₆)alkyl, wherein

20 each of the above is unsubstituted or substituted with 1,
2, 3, 4, or 5 groups that are independently alkyl,
halogen, alkoxy, benzyloxy, hydroxyalkyl,
dihydroxyalkyl, thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂R,
CN, amidinoxime, -NR₈R₉, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-,
25 -C(O)NR₆R₇, -(C₁-C₄)alkyl-C(O)NR₆R₇, amidino, CF₃, or
OCF₃;

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₆
alkyl and phenyl C₁-C₆ alkanoyl; and

R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl, di C₁-
30 C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkanoyl,
phenyl C₁-C₄ alkyl, indazolyl, and phenyl C₁-C₄
alkanoyl.

Embodiment 10. Compounds according to embodiment 4,
wherein

R₅ is phenyl, phenyl(C₁-C₆)alkyl, which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, benzyloxy, thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂R, CN, amidinoxime, -NR₈R₉, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, R₆R₇NC(O)-(C₁-C₄ alkyl)-, R₆R₇NC(O)-(C₅-C₆ alkyl)-, -C(O)NR₆R₇, amidino, CF₃, or OCF₃; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl C₁-C₄ alkyl, phenyl C₁-C₄ alkoxy, or phenyl C₁-C₄ alkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen;

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₆ alkyl and phenyl C₁-C₆ alkanoyl; and

R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl, di C₁-C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₄ alkyl, indazolyl, and phenyl C₁-C₄ alkanoyl.

Embodiment 11. Compounds according to embodiment 10,
wherein

R₅ is phenyl, benzyl or phenethyl, wherein each is optionally substituted with 1, 2, 3, 4, or 5 groups that are

independently C₁-C₆ alkyl, -NR₆R₇, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, -NR₈R₉, halogen, C₁-C₆ alkoxy, CO₂R, -(C₁-C₄ alkyl)-CO₂R, C₁-C₆ thioalkoxy, amidinooxime, C₁-C₆ alkoxycarbonyl, -(C₁-C₄ alkyl)-C₁-C₆ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, -(C₁-C₄ alkyl)-CN, CN, phenyl C₁-C₆ alkoxy, OH, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, R₆R₇N-(C₁-C₆ alkyl)-, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, amidinooxime, -SO₂(C₁-C₆ alkyl), -O-CH₂-O-, -O-CH₂CH₂-O-, phenyl C₁-C₄ alkoxy, or phenyl; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkanoyl, or C₁-C₄ alkoxy, each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

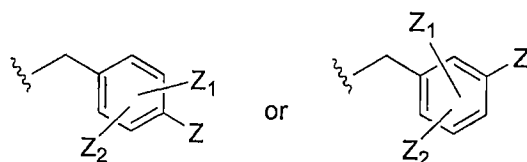
Embodiment 12. Compounds according to embodiment 11, wherein

R₅ is phenyl, benzyl or phenethyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently CN, halogen, C₁-C₄ alkoxy, CF₃, OCF₃, C₁-C₄ alkyl, -NR₈R₉, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, or -C(O)NR₆R₇, wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, C₁-C₄ alkanoyl, or C₁-C₄ alkoxy, each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

Embodiment 13. Compounds according to embodiment 4, wherein

the R₅ group is of the formula:



wherein

Z_1 and Z_2 are independently H, halogen, C_1 - C_4 alkyl, or CO_2R ; and

5 Z is $-C(O)NR_6R_7$, $-(C_1-C_4)alkyl-C(O)NR_6R_7$, $-(C_1-C_4 alkyl)-NR_{15}C(O)R_{18}$, $-NR_6R_7$, $R_6R_7N-(C_1-C_6 alkyl)-$, $-NR_8R_9$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, C_1-C_6 alkyl, CO_2R , or halogen; wherein

10 R_6 and R_7 at each occurrence are independently H, OH, C_1-C_6 alkyl, amino C_1-C_4 alkyl, $NH(C_1-C_6 alkyl)alkyl$, $N(C_1-C_6 alkyl)(C_1-C_6 alkyl)$ C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, C_1-C_6 alkoxy C_1-C_6 alkyl, or $-SO_2(C_1-C_6 alkyl)$ each of which is optionally substituted with 1, 2, or 3 groups that are
15 independently halogen, OH, SH, C_3-C_6 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl, OH, CF_3 , or OCF_3 ;

or

20 R_6 , R_7 , and the nitrogen to which they are attached form a piperidinyll, pyrrolidinyl, piperazinyl, or a morpholinyl, thiomorpholinyl, ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C_1-C_4 alkyl, C_1-C_4 dihydroxyalkyl, or halogen; and

25 R_{18} is C_1-C_6 alkyl optionally substituted with $-O-(C_2-C_6$ alkanoyl, C_1-C_6 hydroxyalkyl, C_1-C_4 dihydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl; amino C_1-C_6 alkyl, mono or dialkylamino C_1-C_6 alkyl.

Embodiment 14. Compounds according to embodiment 4,
30 wherein

R₅ is pyrazolyl (C₁-C₆ alkyl), imidazolyl (C₁-C₆ alkyl),
 thienyl (C₁-C₆ alkyl), furanyl (C₁-C₆ alkyl), piperidinyl (C₁-
 C₆)alkyl, pyrrolidinyl (C₁-C₆)alkyl, imidazolidinyl (C₁-
 C₆)alkyl, piperazinyl (C₁-C₆)alkyl, pyridyl (C₁-C₆)alkyl,
 5 pyrimidyl (C₁-C₆)alkyl, pyridazyl (C₁-C₆)alkyl, pyrazinyl (C₁-
 C₆)alkyl, isoquinolinyl (C₁-C₆)alkyl,
 tetrahydroisoquinolinyl (C₁-C₆)alkyl, indolyl (C₁-C₆)alkyl,
 1H-indazolyl (C₁-C₆)alkyl, dihydroindolyl (C₁-C₆ alkyl),
 dihydroindolon-2-yl (C₁-C₆ alkyl), indolinyl (C₁-C₆ alkyl),
 10 dihydroisoindolyl (C₁-C₆ alkyl), dihydrobenzimidazolyl (C₁-C₆
 alkyl), or dihydrobenzoimidazolonyl (C₁-C₆ alkyl), wherein
 each of the above is unsubstituted or substituted with 1,
 2, 3, 4, or 5 groups that are independently (C₁-
 C₆)alkyl, halogen, (C₁-C₆)alkoxy, (C₁-C₆)hydroxyalkyl,
 15 C₁-C₆ dihydroxyalkyl, phenyl (C₁-C₆)alkoxy, (C₁-
 C₆)thioalkoxy, (C₁-C₆)alkoxycarbonyl, phenyl (C₁-
 C₆)alkoxycarbonyl, OH, CO₂R, CN, amidinoxime, -NR₈R₉,
 -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, -(C₁-C₄
 alkyl)-C(O)NR₆R₇, amidino, piperazinyl, morpholinyl, -
 20 SO₂ (C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆)alkyl, -
 SO₂N(C₁-C₆)alkyl (C₁-C₆)alkyl, (C₁-C₄)haloalkyl, -(C₁-
 C₄ alkyl)-NR₁₅C(O)NR₁₆R₁₇, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈,
 -O-CH₂-O-, -O-CH₂CH₂-O-, or (C₁-C₄)haloalkoxy; wherein
 R₆ and R₇ are independently at each occurrence H,
 25 (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy (C₁-
 C₆)alkyl, (C₁-C₆)alkoxycarbonyl, (C₁-
 C₆)hydroxyalkyl, C₁-C₆ dihydroxyalkyl, -(C₁-
 C₄)alkyl-CO₂-(C₁-C₆)alkyl, (C₁-C₆)alkanoyl,
 phenyl (C₁-C₆)alkyl, phenyl (C₁-C₆)alkoxy, or
 30 phenyl (C₁-C₆)alkanoyl, wherein each of the above
 is unsubstituted or substituted with 1, 2, or 3
 groups that are independently, halogen, (C₁-
 C₄)alkoxy, OH, SH, C₃-C₆ cycloalkyl, NH₂, NH(C₁-

C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), (C₁-C₄)alkyl, CF₃ or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen; and

10 R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

15 In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment 15. Compounds according to embodiment 14,

20 wherein

R₅ is pyrazolyl(C₁-C₆ alkyl), imidazolyl(C₁-C₆ alkyl), benzimidazolyl(C₁-C₆ alkyl), thienyl(C₁-C₆ alkyl), pyrimidyl(C₁-C₆)alkyl, indolyl(C₁-C₆ alkyl), dihydroindolyl(C₁-C₆ alkyl), dihydroisoindolyl(C₁-C₆ alkyl), dihydroindolon-2-yl(C₁-C₆ alkyl), pyridinyl(C₁-C₆ alkyl), piperazinyl(C₁-C₆ alkyl), or pyrazinyl(C₁-C₆ alkyl) each of which is optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, halogen, -C(O)NR₆R₇, - (C₁-C₄ alkyl)-C(O)NR₆R₇, C₁-C₆ alkoxycarbonyl, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, haloalkyl, C₁-C₆ alkanoyl,

30

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups

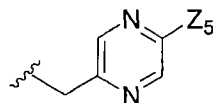
that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 16. Compounds according to embodiment 15, wherein

R₅ is of the formula:



wherein

Z₅ is C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, C₁-C₆ alkoxy carbonyl, R₆R₇N-(C₁-C₆ alkyl)-, -NR₆R₇, CF₃, or C₁-C₆ alkanoyl, wherein

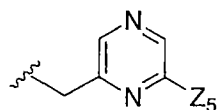
R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 17. Compounds according to embodiment 15, wherein

R₅ is of the formula:



wherein

Z₅ is C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, C₁-C₆ alkoxy carbonyl, R₆R₇N-(C₁-C₆ alkyl)-, -NR₆R₇, CF₃, or C₁-C₆ alkanoyl, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

R₆, R₇, and the nitrogen to which they are attached form a piperidiny, pyrrolidiny, piperaziny, or a morpholiny ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 18. Compounds according to either embodiment 16 or 17, wherein

Z₅ is C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, halogen, C₁-C₆ alkoxy carbonyl, CF₃, or C₁-C₆ alkanoyl.

Embodiment 19. Compounds according to either embodiment 16 or 17, wherein

Z₅ is C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, or -NR₆R₇, CF₃, or C₁-C₄ alkanoyl, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

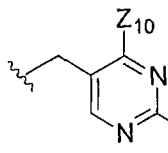
R_6 , R_7 , and the nitrogen to which they are attached form a piperidiny1, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C_1 - C_4 alkyl, C_1 - C_4 dihydroxyalkyl, or halogen.

Embodiment 20. Compounds according to embodiment 19, wherein

Z_5 is $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, cyclopropyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 21. Compounds according to embodiment 15, wherein



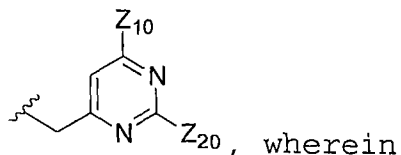
R_5 is of the formula:

Z_{10} is H or methyl; and

Z_{20} is hydroxy(C_1 - C_4)alkyl, C_1 - C_4 dihydroxyalkyl, OH, halogen, haloalkyl, (C_1 - C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 22. Compounds according to embodiment 15, wherein



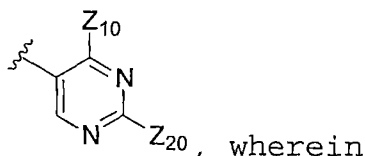
R_5 is of the formula:

Z_{10} is H or methyl; and

Z_{20} is hydroxy(C_1 - C_4)alkyl, C_1 - C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1 - C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6$ alkyl)-, $-(C_1-C_4$ alkyl)- $C(O)NR_6R_7$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 23. Compounds according to embodiment 15, wherein



R_5 is of the formula:

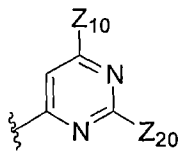
Z_{10} is H or methyl; and

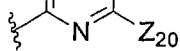
Z_{20} is hydroxy(C_1 - C_4)alkyl, C_1 - C_4 dihydroxyalkyl, OH, halogen, haloalkyl, (C_1 - C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6$ alkyl)-, $-(C_1-C_4$ alkyl)- $C(O)NR_6R_7$, or $-C(O)NR_6R_7$,

wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 24. Compounds according to embodiment 15, wherein



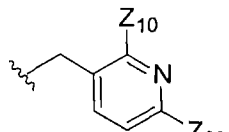
R₅ is of the formula: , wherein

Z₁₀ is H or methyl; and

Z₂₀ is hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, CF₃, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, - (C₁-C₄ alkyl)-C(O)NR₆R₇, or -C(O)NR₆R₇, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy.

Embodiment 25. Compounds according to embodiment 15, wherein



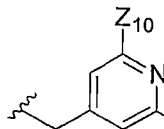
R₅ is of the formula:

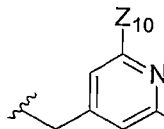
Z₁₀ is H or methyl; and

Z₂₀ is hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, haloalkyl, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, - (C₁-C₄ alkyl)-C(O)NR₆R₇, or -C(O)NR₆R₇, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy.

Embodiment 26. Compounds according to embodiment 15, wherein



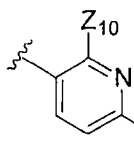
R₅ is of the formula: , wherein

Z_{10} is H or methyl; and

Z_{20} is hydroxy(C_1 - C_4)alkyl, C_1 - C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1 - C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6$ alkyl)-, $-(C_1-C_4$ alkyl)- $C(O)NR_6R_7$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 27. Compounds according to embodiment 15, wherein



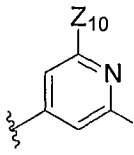
R_5 is of the formula:

Z_{10} is H or methyl; and

Z_{20} is hydroxy(C_1 - C_4)alkyl, C_1 - C_4 dihydroxyalkyl, OH, halogen, haloalkyl, (C_1 - C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6$ alkyl)-, $-(C_1-C_4$ alkyl)- $C(O)NR_6R_7$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 28. Compounds according to embodiment 15, wherein



R_5 is of the formula:

Z_{10} is H or methyl; and

Z_{20} is hydroxy(C_1 - C_4)alkyl, C_1 - C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1 - C_4)alkyl, OCF_3 , $-NR_6R_7$, R_6R_7N -(C_1 - C_6 alkyl)-, $-(C_1$ - C_4 alkyl)- $C(O)NR_6R_7$, or $-C(O)NR_6R_7$, wherein R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy, carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 29. Compounds according to embodiment 4, wherein

R_5 is phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1$ - C_4 alkyl)- $C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1$ - C_6 alkyl), C_1 - C_6 hydroxyalkyl, dihydroxyalkyl, halogen, C_1 - C_4 alkoxy, CO_2R , OH, C_1 - C_6 alkoxy, carbonyl, CF_3 , $-(C_1$ - C_4 alkyl)- $NR_{15}C(O)NR_{16}R_{17}$, $-(C_1$ - C_4 alkyl)- $NR_{15}C(O)R_{18}$; wherein R_{15} is H or C_1 - C_6 alkyl;

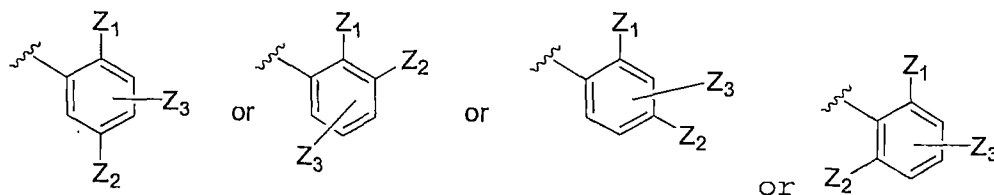
R_{16} and R_{17} are independently H or C_1 - C_6 alkyl; or

R_{16} , R_{17} , and the nitrogen to which they are attached form a morpholinyl ring; and

R_{18} is C_1 - C_6 alkyl optionally substituted with $-O$ -(C_2 - C_6 alkanoyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 dihydroxyalkyl, C_1 - C_6 alkoxy, C_1 - C_6 alkoxy C_1 - C_6 alkyl; amino C_1 - C_6 alkyl, mono or dialkylamino C_1 - C_6 alkyl.

Embodiment 30. Compounds according to embodiment 29, wherein

R_5 is of the formula:



Z_1 is H, halogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 hydroxyalkyl, C_1 - C_4 dihydroxyalkyl, or C_1 - C_4 alkoxy; and

Z_2 is C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, halogen, C_1 - C_4 alkoxy, CO_2R , OH, C_1-C_6 alkoxy carbonyl, or C_1 - C_4 haloalkyl;

Z_3 is H, C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, halogen, C_1 - C_4 alkoxy, CO_2R , OH, C_1-C_6 alkoxy carbonyl, or C_1 - C_4 haloalkyl;

and wherein

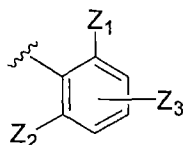
R_6 and R_7 at each occurrence are independently H, OH, C_1 - C_6 alkyl, amino C_1 - C_4 alkyl, $NH(C_1-C_6 \text{ alkyl})$ alkyl, $N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$ C_1 - C_6 alkyl, C_1 - C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, C_1-C_6 alkoxy C_1 - C_6 alkyl, $-SO_2(C_1-C_6 \text{ alkyl})$, $-SO_2NH_2$, $-SO_2NH(C_1-C_6 \text{ alkyl})$, $-SO_2N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, or C_1 - C_6 alkanoyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C_3 - C_6 cycloalkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkyl, OH, CF_3 , or OCF_3 .

In this embodiment, it is preferred that at least one of Z_1 , Z_2 , and Z_3 is not hydrogen.

Embodiment 31. Compounds according to embodiment 30,

wherein

R_5 is of the formula:



wherein

Z_1 is H, halogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 hydroxyalkyl, C_1 - C_4 dihydroxyalkyl, or C_1 - C_4 alkoxy; and

Z_2 is C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , OH , C_1-C_6 alkoxycarbonyl, or C_1-C_4 haloalkyl;

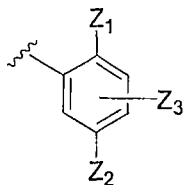
5 Z_3 is H , C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , OH , C_1-C_6 alkoxycarbonyl, or C_1-C_4 haloalkyl, and wherein

10 R_6 and R_7 at each occurrence are independently H , OH , C_1-C_6 alkyl, amino C_1-C_4 alkyl, $NH(C_1-C_6 \text{ alkyl})alkyl$, $N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$ C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, C_1-C_6 alkoxy C_1-C_6 alkyl, $-SO_2(C_1-C_6 \text{ alkyl})$, $-SO_2NH_2$, $-SO_2NH(C_1-C_6 \text{ alkyl})$, $-SO_2N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, or C_1-C_6 alkanoyl,
 15 each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH , SH , C_3-C_6 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl, OH , CF_3 , or OCF_3 .

In this embodiment, it is preferred that at least one of
 20 Z_1 , Z_2 , and Z_3 is not hydrogen.

Embodiment 32. Compounds according to embodiment 30, wherein

R_5 is of the formula:



25 wherein

Z_1 is H , halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 hydroxyalkyl, C_1-C_4 dihydroxyalkyl, or C_1-C_4 alkoxy; and

30 Z_2 is C_1-C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6

dihydroxyalkyl, halogen, C₁-C₄ alkoxy, CO₂R, OH, C₁-C₆ alkoxy carbonyl, or C₁-C₄ haloalkyl;

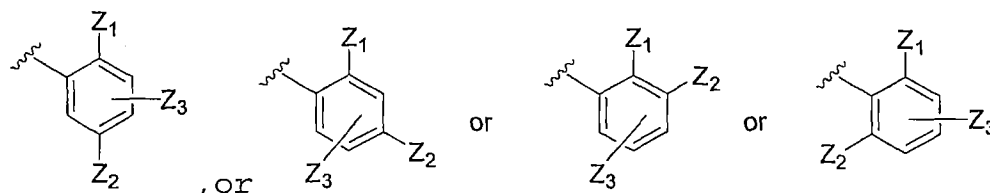
Z₃ is H, C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, -NR₆R₇, NR₆R₇(C₁-C₆ alkyl), C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, halogen, C₁-C₄ alkoxy, CO₂R, OH, C₁-C₆ alkoxy carbonyl, or C₁-C₄ haloalkyl, and wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or C₁-C₆ alkanoyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

In this embodiment, it is preferred that at least one of Z₁, Z₂, and Z₃ is not hydrogen.

Embodiment 33. Compounds according to embodiment 29, wherein

R₅ is either



wherein

Z₁ is H, halogen, C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ dihydroxyalkyl, or C₁-C₄ alkoxy; and Z₂ is C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, -NR₆R₇, NR₆R₇(C₁-C₆ alkyl), C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, halogen, C₁-C₄ alkoxy, CO₂R, C₁-C₆

alkoxycarbonyl, $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)NR_{16}R_{17}$, or $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)R_{18}$;

Z_3 is H, C_1-C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$,
 $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6
 5 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , C_1-C_6
 alkoxycarbonyl, $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)NR_{16}R_{17}$, or $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)R_{18}$;

R_6 , R_7 , and the nitrogen to which they are attached form a
 piperidiny, pyrrolidiny, piperaziny, or a
 10 morpholiny ring optionally substituted with 1 or 2
 groups that are independently alkyl, hydroxy,
 hydroxy C_1-C_4 alkyl, C_1-C_4 dihydroxyalkyl, or halogen;

R_{15} is H or C_1-C_6 alkyl;

R_{16} and R_{17} are independently H or C_1-C_6 alkyl; or

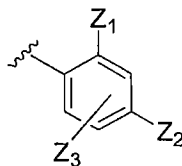
15 R_{16} , R_{17} , and the nitrogen to which they are attached form
 a morpholiny ring; and

R_{18} is C_1-C_6 alkyl optionally substituted with $-O-(C_2-C_6$
 alkanoyl, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl,
 C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl; amino C_1-C_6
 20 alkyl, mono or dialkylamino C_1-C_6 alkyl.

In this embodiment, it is preferred that at least one of
 Z_1 , Z_2 , and Z_3 is not hydrogen.

Embodiment 34. Compounds according to embodiment 33,
 25 wherein

R_5 is of the formula:



Z_1 is H, halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4
 30 hydroxyalkyl, C_1-C_4 dihydroxyalkyl, or C_1-C_4 alkoxy; and

Z_2 is C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$,
 $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6
 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , C_1-C_6
 alkoxycarbonyl, $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)NR_{16}R_{17}$, or $-(C_1-C_4$
 5 $\text{alkyl})-NR_{15}C(O)R_{18}$;

Z_3 is H, C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$,
 $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6
 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , C_1-C_6
 alkoxycarbonyl, $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)NR_{16}R_{17}$, or $-(C_1-C_4$
 10 $\text{alkyl})-NR_{15}C(O)R_{18}$;

R_6 , R_7 , and the nitrogen to which they are attached form a
 piperidinyll, pyrrolidinyl, piperazinyl, or a
 morpholinyl ring optionally substituted with 1 or 2
 groups that are independently alkyl, hydroxy,
 15 hydroxy C_1 - C_4 alkyl, C_1 - C_4 dihydroxyalkyl, or halogen;

R_{15} is H or C_1 - C_6 alkyl;

R_{16} and R_{17} are independently H or C_1 - C_6 alkyl; or

R_{16} , R_{17} , and the nitrogen to which they are attached form
 a morpholinyl ring; and

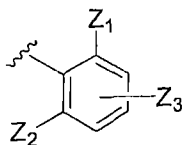
R_{18} is C_1 - C_6 alkyl optionally substituted with $-O-(C_2-C_6$
 20 alkanoyl , C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl,
 C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl; amino C_1-C_6
 alkyl, mono or dialkylamino C_1-C_6 alkyl.

In this embodiment, it is preferred that at least one of

25 Z_1 , Z_2 , and Z_3 is not hydrogen.

Embodiment 35. Compounds according to embodiment 33,
 wherein

R_5 is of the formula:



wherein

Z_1 is H, halogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 hydroxyalkyl, C_1 - C_4 dihydroxyalkyl, or C_1 - C_4 alkoxy; and

Z_2 is C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , C_1-C_6 alkoxy carbonyl, $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)NR_{16}R_{17}$, or $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)R_{18}$;

Z_3 is H, C_1 - C_4 alkyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $NR_6R_7(C_1-C_6 \text{ alkyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, halogen, C_1-C_4 alkoxy, CO_2R , C_1-C_6 alkoxy carbonyl, $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)NR_{16}R_{17}$, or $-(C_1-C_4 \text{ alkyl})-NR_{15}C(O)R_{18}$;

R_6 , R_7 , and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C_1 - C_4 alkyl, C_1 - C_4 dihydroxyalkyl, or halogen;

R_{15} is H or C_1 - C_6 alkyl;

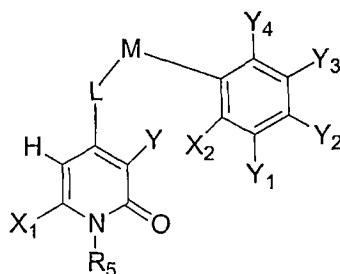
R_{16} and R_{17} are independently H or C_1 - C_6 alkyl; or

R_{16} , R_{17} , and the nitrogen to which they are attached form a morpholinyl ring; and

R_{18} is C_1 - C_6 alkyl optionally substituted with $-O-(C_2-C_6 \text{ alkanoyl})$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl; amino C_1-C_6 alkyl, mono or dialkylamino C_1-C_6 alkyl.

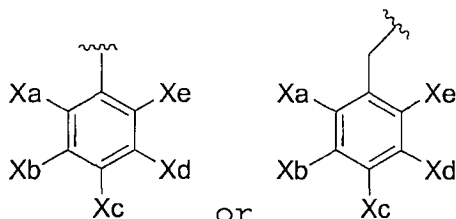
In this embodiment, it is preferred that at least one of Z_1 , Z_2 , and Z_3 is not hydrogen.

Embodiment 36. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

L and M are independently selected from -O-, -CH₂-, -S-, -NR-, -N(R)-N(R)-, C(=O)-, -SO₂-;



5 R₅ is or , wherein

X₁, X₂, X_a, X_b, X_c, X_d, and X_e at are independently selected from -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, -NR₆R₇, hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, H, OH, halogen, haloalkyl, alkyl, haloalkoxy, heteroaryl, heterocycloalkyl, C₃-C₇ cycloalkyl, R₆R₇N-(C₁-C₆ alkyl)-, -CO₂-(C₁-C₆)alkyl, -N(R)C(O)NR₆R₇, -N(R)C(O)-(C₁-C₆)alkoxy, CO₂R-(C₁-C₆ alkyl)-, or -SO₂NR₆R₇; wherein the heteroaryl and heterocycloalkyl groups are optionally substituted with -NR₆R₇, -C(O)NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, C₁-C₆ alkyl, C₁-C₆ alkoxy, or halogen; or

R₅ is heteroaryl or heteroarylalkyl, wherein the heteroaryl and heteroaryl groups are optionally substituted with 1, 2, 3, or 4 groups that are independently -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, -NR₆R₇, hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, H, OH, halogen, haloalkyl, alkyl, haloalkoxy, R₆R₇N-(C₁-C₆ alkyl)-, -CO₂-(C₁-C₆)alkyl, -N(R)C(O)NR₆R₇, or -N(R)C(O)-(C₁-C₆)alkoxy; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, C₁-C₄

dihydroxyalkyl, C₁-C₆ thiohydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

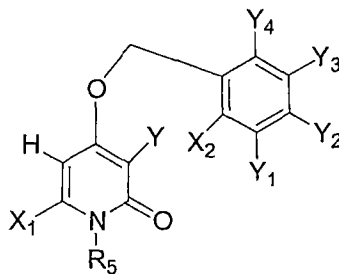
R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen;

R at each occurrence is independently H or C₁-C₆ alkyl;

and

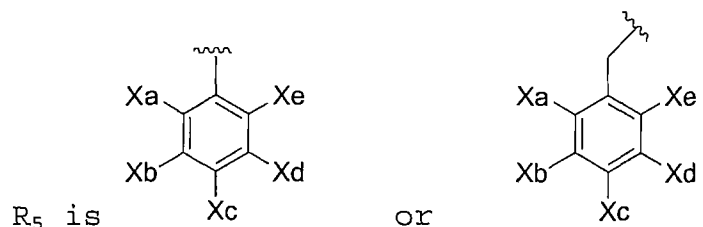
Y, Y₁, Y₂, Y₃, and Y₄ are independently selected from H, halogen, alkyl, carboxaldehyde, hydroxyalkyl, dihydroxyalkyl, alkenyl, alkynyl, CN, alkanoyl, alkoxy, alkoxyalkyl, haloalkyl, and carboxyl.

Embodiment 37. Compounds according to embodiment 36 of the formula



or a pharmaceutically acceptable salt thereof.

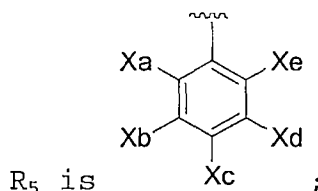
Embodiment 38. Compounds according to embodiment 37,
wherein



Embodiment 39. Compounds according to embodiment 31,
wherein

Y₂, Y₄, and Y are independently halogen; and
Y₁ and Y₃ are both hydrogen.

Embodiment 40. Compounds according to embodiment 39,
wherein



X₁ and X₂ are independently H, methyl, NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, or -(C₁-C₄ alkyl)-morpholinyl; and

X_a and X_e are independently halogen, NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), methyl, or hydrogen.

In this embodiment, it is preferred that one of X_a and X_e is not hydrogen.

Embodiment 41. Compounds according to embodiment 40,
wherein

one of X_b and X_c is hydrogen and the other is $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, $-C(O)NR_6R_7$, $-SO_2NR_6R_7$, or halogen; where

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 42. Compounds according to embodiment 41, wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃.

Embodiment 43. Compounds according to embodiment 42, wherein

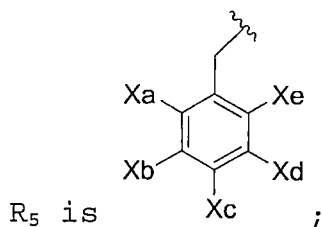
X_a is hydrogen, methyl, fluorine, or chlorine;

5 X_c and X_d are both hydrogen;

X_b is $-NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, $-C(O)NR_6R_7$; wherein

10 R_6 and R_7 are independently at each occurrence H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_4 dihydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, or C_1-C_6 alkanoyl, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently OH, SH, halogen, or C_3-C_6 cycloalkyl.

15 Embodiment 44. Compounds according to embodiment 39, wherein



X_a is H, fluoro, chloro, or methyl;

X_e is hydrogen, halogen, or methyl; and

20 X_b is H;

X_d is H or halogen;

Embodiment 45. Compounds according to embodiment 44, wherein

25 X_c is $-SO_2NR_6R_7$, or halogen; wherein

R_6 and R_7 are independently at each occurrence H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, C_1-C_6 alkoxy carbonyl, OH, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, $-(C_1-C_4)\text{alkyl}-CO_2\text{-alkyl}$, pyridyl C_1-C_6

alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidiny1 C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidiny1, pyrrolidiny1, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen; or

X_c is fluoro, chloro, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)(C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or piperazinyl, wherein the piperazinyl group is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 46. Compounds according to embodiment 44, wherein

X_c is -C(O)NR₆R₇, -(C₁-C₆ alkyl)-C(O)NR₆R₇, -NR₆R₇, or R₆R₇N-(C₁-C₆ alkyl)-; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, C₁-C₆ dihydroxyalkyl, C₁-C₆ dihydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl,

wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, -NH₂, -NH(alkyl), -N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen.

Embodiment 47. Compounds according to embodiment 46, wherein

R₆ is hydrogen; and

R₇ is C₁-C₆ alkyl or C₁-C₆ alkanoyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), OH, SH, cyclopropyl, or C₁-C₄ alkoxy;

Embodiment 48. Compounds according to embodiment 47, wherein

X_c is -C(O)NR₆R₇.

Embodiment 49. Compounds according to embodiment 47, wherein

X_c is NR₆R₇, or R₆R₇N-(C₁-C₆ alkyl)-.

Embodiment 50. Compounds according to embodiment 38, wherein

X_a is hydrogen;

two of X_b , X_c , and X_d are hydrogen and the other is $-C(O)NR_6R_7$, $-(C_1-C_6 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$ or $-CO_2-(C_1-C_6)\text{alkyl}$; wherein

R_6 and R_7 are independently at each occurrence H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, C_1-C_6 alkoxycarbonyl, OH, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, $-(C_1-C_4)\text{alkyl}-CO_2\text{-alkyl}$, pyridyl C_1-C_6 alkyl, C_1-C_6 alkanoyl, benzyl, phenyl C_1-C_6 alkoxy, or phenyl C_1-C_6 alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, piperidinyl C_1-C_6 alkyl, morpholinyl C_1-C_6 alkyl, piperazinyl C_1-C_6 alkyl, OH, NH_2 , $NH(\text{alkyl})$, $N(\text{alkyl})(\text{alkyl})$, $-O-C_1-C_4$ alkanoyl, C_1-C_4 alkyl, CF_3 , or OCF_3 ; or

R_6 , R_7 , and the nitrogen to which they are attached form a morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, hydroxy, hydroxy C_1-C_4 alkyl, C_1-C_4 dihydroxyalkyl, or halogen; and

X_e is hydrogen, methyl, C_1-C_2 alkoxy, or halogen.

Embodiment 51. Compounds according to embodiment 50, wherein

X_b is $-C(O)NR_6R_7$, $-(C_1-C_6 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, or $R_6R_7N-(C_1-C_6 \text{ alkyl})-$ wherein

R_6 is hydrogen or C_1-C_4 alkyl;

R_7 is OH, C_1-C_6 alkyl or C_1-C_6 alkanoyl, wherein the alkyl and alkanoyl groups substituted with 1, 2, or 3 groups that are independently NH_2 , $NH(C_1-C_6 \text{ alkyl})$, $N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, C_3-C_6 cycloalkyl, OH, or C_1-C_4 alkoxy.

Embodiment 52. Compounds according to embodiment 38, wherein

X_a is halogen or methyl;

X_b is H, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, or -CO₂-(C₁-C₆)alkyl;

X_c is -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, halogen, -CO₂-(C₁-C₆)alkyl, NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or piperazinyl, wherein the piperazinyl group is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, C₁-C₄ dihydroxyalkyl, or halogen;

X_d is hydrogen;

X_e is H, methyl, NH₂, NH(C₁-C₆ alkyl) or N(C₁-C₆ alkyl)(C₁-C₆ alkyl).

Embodiment 53. Compounds according to embodiment 38, wherein

X₁, X₂, X_a, X_b, X_c, X_d, and X_e are independently selected from H, OH, halogen, CF₃, alkyl, OCF₃, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, thienyl, furyl, pyrrolyl, piperidinyl, piperazinyl, or C₃-C₇ cycloalkyl, wherein each of the above is optionally substituted with -NR₆R₇, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, C₁-C₆ alkyl, C₁-C₆ alkoxy, or halogen.

Embodiment 54. Compounds according to embodiment 37, wherein

R₅ is a heteroaryl or heteroarylalkyl group, where each heteroaryl is pyrazolyl, imidazolyl, furanyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrazolyl, imidazolyl, dihydroindolyl, dihydroisoindolyl, indolon-2-yl, quinolinyl, isoquinolinyl, tetrahydroisoquinolinyl,

dihydroisoquinolinyl, or indolyl, each of which is optionally substituted with 1, 2, 3, or 4 groups that are independently $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $-NR_6R_7$, hydroxy(C_1-C_4)alkyl, C_1-C_4 dihydroxyalkyl, hydrogen, hydroxy, halogen, haloalkyl, alkyl, haloalkoxy, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, $-CO_2-(C_1-C_6)alkyl$, $-N(R)C(O)NR_6R_7$, or $-N(R)C(O)-(C_1-C_6)alkoxy$; wherein

R_6 and R_7 are independently at each occurrence H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, C_1-C_6 alkoxycarbonyl, OH, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, C_1-C_6 thiohydroxyalkyl, $-(C_1-C_4)alkyl-CO_2-alkyl$, pyridyl C_1-C_6 alkyl, C_1-C_6 alkanoyl, benzyl, phenyl C_1-C_6 alkoxy, or phenyl C_1-C_6 alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, piperidinyl C_1-C_6 alkyl, morpholinyl C_1-C_6 alkyl, piperazinyl C_1-C_6 alkyl, OH, SH, NH_2 , $NH(alkyl)$, $N(alkyl)(alkyl)$, $-O-C_1-C_4$ alkanoyl, C_1-C_4 alkyl, CF_3 , or OCF.

Embodiment 55. Compounds according to embodiment 54, wherein

Y_2 , Y_4 , and Y are independently halogen; and

Y_1 and Y_3 are both hydrogen.

Embodiment 56. Compounds according to embodiment 55, wherein

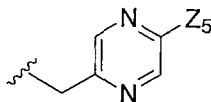
X_1 and X_2 are independently H, methyl, $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, C_1-C_6 hydroxyalkyl, C_1-C_6 dihydroxyalkyl, or $-(C_1-C_4 \text{ alkyl})-morpholinyl$.

Embodiment 57. Compounds according to embodiment 56, wherein

R₅ is pyridyl C₁-C₆ alkyl, pyrimidinyl C₁-C₆ alkyl, or pyrazinyl C₁-C₆ alkyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, CF₃, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, or -C(O)NR₆R₇.

Embodiment 58. Compounds according to embodiment 57, wherein

R₅ is of the formula:



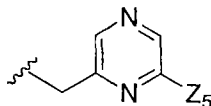
wherein

Z₅ is hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, CF₃, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, -(C₁-C₄ alkyl)-C(O)NR₆R₇, or -C(O)NR₆R₇, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxycarbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy.

Embodiment 59. Compounds according to embodiment 57, wherein

R₅ is of the formula:



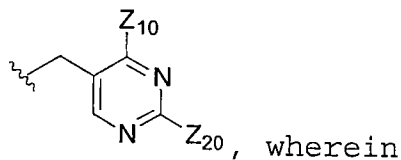
wherein

Z₅ is hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, CF₃, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, -(C₁-C₄ alkyl)-C(O)NR₆R₇, or -C(O)NR₆R₇, wherein

R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

5

Embodiment 60. Compounds according to embodiment 57, wherein



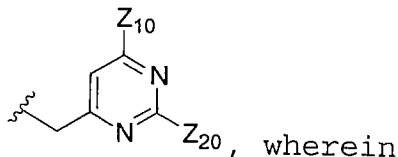
R_5 is of the formula:

Z_{10} is H or methyl; and

10 Z_{20} is $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, hydroxy(C_1-C_4)alkyl, C_1-C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1-C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-C(O)NR_6R_7$, wherein

15 R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 61. Compounds according to embodiment 57, wherein



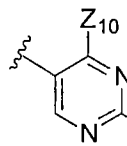
20 R_5 is of the formula:

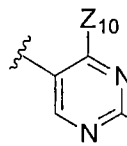
Z_{10} is H or methyl; and

Z_{20} is $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, hydroxy(C_1-C_4)alkyl, C_1-C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1-C_4)alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-C(O)NR_6R_7$, wherein

25 R_6 and R_7 at each occurrence are independently H, C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1 - C_4 alkoxy carbonyl, halogen, C_3 - C_6 cycloalkyl, OH, SH, or C_1 - C_4 alkoxy.

Embodiment 62. Compounds according to embodiment 57,
wherein



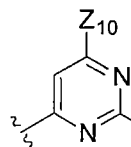
R₅ is of the formula: , wherein

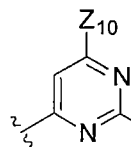
Z₁₀ is H or methyl; and

Z₂₀ is -(C₁-C₄ alkyl)-C(O)NR₆R₇, hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, CF₃, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, or -C(O)NR₆R₇, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy.

Embodiment 63. Compounds according to embodiment 57,
wherein



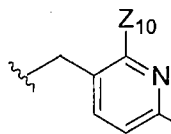
R₅ is of the formula: , wherein

Z₁₀ is H or methyl; and

Z₂₀ is -(C₁-C₄ alkyl)-C(O)NR₆R₇, hydroxy(C₁-C₄)alkyl, C₁-C₄ dihydroxyalkyl, OH, halogen, CF₃, (C₁-C₄)alkyl, OCF₃, -NR₆R₇, R₆R₇N-(C₁-C₆ alkyl)-, or -C(O)NR₆R₇, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy.

Embodiment 64. Compounds according to embodiment 57,
wherein



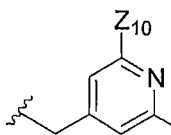
R_5 is of the formula:

Z_{10} is H or methyl; and

Z_{20} is $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, hydroxy (C_1-C_4) alkyl, C_1-C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1-C_4) alkyl, OCF_3 ,
 5 $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1-C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxy carbonyl, halogen, C_3-C_6 cycloalkyl, OH, SH, or C_1-C_4 alkoxy.

10 Embodiment 65. Compounds according to embodiment 57, wherein



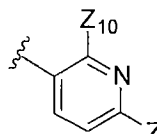
R_5 is of the formula:

Z_{10} is H or methyl; and

15 Z_{20} is $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, hydroxy (C_1-C_4) alkyl, C_1-C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1-C_4) alkyl, OCF_3 ,
 $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1-C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxy carbonyl, halogen,
 20 C_3-C_6 cycloalkyl, OH, SH, or C_1-C_4 alkoxy.

Embodiment 66. Compounds according to embodiment 57, wherein



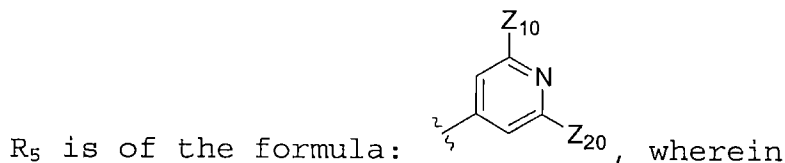
25 R_5 is of the formula:

Z_{10} is H or methyl; and

Z_{20} is $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, hydroxy (C_1-C_4) alkyl, C_1-C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1-C_4) alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1-C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxy carbonyl, halogen, C_3-C_6 cycloalkyl, OH, SH, or C_1-C_4 alkoxy.

Embodiment 67. Compounds according to embodiment 57, wherein



Z_{10} is H or methyl; and

Z_{20} is $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, hydroxy (C_1-C_4) alkyl, C_1-C_4 dihydroxyalkyl, OH, halogen, CF_3 , (C_1-C_4) alkyl, OCF_3 , $-NR_6R_7$, $R_6R_7N-(C_1-C_6 \text{ alkyl})-$, or $-C(O)NR_6R_7$, wherein

R_6 and R_7 at each occurrence are independently H, C_1-C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxy carbonyl, halogen, C_3-C_6 cycloalkyl, OH, SH, or C_1-C_4 alkoxy.

Embodiment A7. Compounds according to embodiment 1 wherein

R_1 is H, halogen, alkyl optionally substituted with C_1-C_4 alkoxy carbonyl, C_2-C_6 alkenyl optionally substituted with C_1-C_4 alkoxy carbonyl, C_2-C_4 alkynyl, C_1-C_4 haloalkyl, carboxaldehyde, C_1-C_4 hydroxyalkyl, phenyl (C_1-C_6) alkoxy, benzyl, phenethyl, phenpropyl, CN, or phenyl (C_1-C_6) alkanoyl,

wherein the phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, CF₃, OCF₃ or CO₂H;

5 R₂ is OH, benzyloxy, phenyloxy, phenyloxy(C₁-C₆)alkyl, phenyl (C₁-C₄) thioalkoxy, -OC(O)NH(CH₂)_nphenyl, -OC(O)N(alkyl)(CH₂)_nphenyl, di(C₁-C₆)alkylamino, C₂-C₆ alkynyl, pyridyl, pyrimidyl, pyridazyl, pyrazolyl, imidazolyl, pyrrolyl, tetrahydroquinoliny, 10 tetrahydroisoquinoliny, tetrazolyl, pyrazinyl, benzimidazolyl, triazinyl, tetrahydrofuryl, piperidinyl, hexahydropyrimidinyl, thiazolyl, thienyl, or CO₂H, wherein n is 0, 1, 2, 3, 4, 5 or 6; each of the above is unsubstituted or substituted with 1, 15 2, 3, 4, or 5 groups that are independently halogen, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, pyridyl, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, or NR₆R₇-(C₁-C₆ alkyl)-,

R₄ is H, alkyl optionally substituted with one or two groups 20 that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenyl(C₁-C₆)alkoxy, phenyl(C₁-C₆)alkyl, hydroxyalkyl, wherein the phenyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are 25 independently halogen, hydroxy, alkoxy, alkyl, nitro, CF₃, or OCF₃; and

R₅ is phenyl(C₁-C₆)alkyl, (C₁-C₆)alkyl, phenyl, piperidinyl(C₁-C₆) alkyl, thienyl(C₁-C₆) alkyl, indolyl, quinoliny, isoquinoliny, isoindolyl, indol-2-onyl, indazolyl, 30 indolyl (C₁-C₆) alkyl, quinoliny(C₁-C₆) alkyl, isoquinoliny(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, naphthyl(C₁-C₆)alkyl, pyridyl(C₁-

C₆)alkyl, pyrimidyl(C₁-C₆)alkyl, pyrazinyl(C₁-C₆)alkyl, or wherein

each of the above is unsubstituted or substituted with 1,

2, 3, 4, or 5 groups that are independently alkyl,

5 halogen, alkoxy, benzyloxy, thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂H, CN, amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, CF₃, or OCF₃;

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₆ alkyl and phenyl C₁-C₆ alkanoyl; and

10 R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl, di C₁-C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₄ alkyl, indazolyl, and phenyl C₁-C₄ alkanoyl.

In this embodiment, it is preferred that when R₂ is 15 benzyloxy, R₄ is H, and R₅ is benzyl or methyl, R₁ is not hydrogen; and

no more than two of R₁, R₂, R₄, and R₅ are simultaneously hydrogen.

20 Embodiment A8. Compounds according to embodiment A7 wherein

R₁ is H, halogen, C₁-C₄ alkyl optionally substituted with C₁-C₄ alkoxy carbonyl, C₂-C₄ alkenyl optionally substituted with C₁-C₄ alkoxy carbonyl, C₂-C₄ alkynyl, or carboxaldehyde;

25 R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, phenyl (C₁-C₄) thioalkoxy, or pyridyl; wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, 30 pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-.

Embodiment A9. Compounds according to embodiment A7 wherein

R₄ is H, (C₁-C₆)alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenyl(C₁-C₆)alkoxy, or hydroxy(C₁-C₆)alkyl, wherein

5 the phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkyl, nitro, CF₃, OCF₃; and

R₅ is benzyl, phenethyl, phenpropyl, phenbutyl, (C₁-C₆)alkyl, 10 phenyl, pyridyl, pyrimidyl, indolyl, indazolyl, indolyl (C₁-C₆) alkyl, naphthyl(C₁-C₆)alkyl, thienyl(C₁-C₆)alkyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-C₆)alkyl, or pyrazinyl(C₁-C₆)alkyl, and wherein each of the above is unsubstituted or substituted with 1, 15 2, or 3 groups that are independently alkyl, halogen, alkoxy, benzyloxy, thioalkoxy, -CO₂(C₁-C₅ alkyl), CF₃, OCF₃, CO₂H, CN, amidinoxime.

In this embodiment, it is preferred that when R₂ is benzyloxy, R₄ is H, and R₅ is benzyl or methyl, R₁ is not 20 hydrogen; and

no more than two of R₁, R₂, R₄, and R₅ are simultaneously hydrogen.

Embodiment A10. Compounds according to embodiment A7, 25 wherein

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenyl(C₁-C₆)alkoxy, benzyl, phenethyl, phenpropyl, or 30 hydroxy(C₁-C₆)alkyl, wherein

the phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen,

hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkyl, nitro, CF₃, OCF₃;
and

R₅ is indolyl, quinolinyl, isoquinolinyl, isoindolyl, indol-2-onyl, indolyl(C₁-C₆) alkyl, quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, or amidinooxime; wherein

R₆ and R₇ are independently at each occurrence H, alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkanoyl, phenylalkyl, phenylalkoxy, or phenylalkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, hydroxy, C₁-C₄ alkoxy, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A11. Compounds according to embodiment A7 wherein

R₁ is chloro, bromo, iodo, or H; and

R₅ is benzyl, phenethyl, phenpropyl, phenyl, quinolinyl, indolyl, isoquinolinyl, isoindolyl, indol-2-onyl, indolyl(C₁-C₆) alkyl, quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, piperidinyl C₁-C₄ alkyl, thienyl C₁-C₄ alkyl, -CH₂-pyridyl, or pyridyl, each of which is

unsubstituted or substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, NR₈R₉, NR₆R₇, C₁-C₄ alkyl, -C(O)NR₆R₇, and amidinooxime; wherein

R₆ and R₇ are independently at each occurrence H, alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkanoyl, phenylalkyl, phenylalkoxy, or phenylalkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, hydroxy, C₁-C₄ alkoxy, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A12. Compounds according to embodiment A11, wherein

R₅ is benzyl, phenethyl, phenpropyl, or phenyl, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, NR₈R₉, NR₆R₇, C₁-C₄ alkyl, -C(O)NR₆R₇, and amidinooxime.

Embodiment A13. Compounds according to embodiment A11, wherein

R₅ is quinolinyl, indolyl, isoquinolinyl, isoindolyl, indol-2-onyl, indolyl(C₁-C₆) alkyl, quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, piperidinyl C₁-C₄ alkyl, thienyl C₁-C₄

alkyl, -CH₂-pyridyl, or pyridyl, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, NR₈R₉, NR₆R₇ C₁-C₄ alkyl, -C(O)NR₆R₇, and amidinoxime.

Embodiment A14. Compounds according to any one of embodiments A11, A12, or A13 wherein

10 R₂ is benzyloxy, or phenethyloxy;
each of the above is unsubstituted or substituted with 1, 2, or 3, groups that are independently -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, fluoro, chloro, bromo, CF₃, or (C₁-C₄)alkyl.

15 Embodiment A15. Compounds according to any one of embodiments A11, A12 or A13 wherein

R₂ is phenyloxy(C₁-C₆)alkyl, wherein the phenyl group is unsubstituted or substituted with 1, 2, or 3, groups that are independently -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, fluoro, chloro, bromo, CF₃, or (C₁-C₄)alkyl.

Embodiment A16. Compounds according to embodiment A1, wherein

25 R₁ is H, halogen, C₁-C₄ alkyl optionally substituted with C₁-C₄ alkoxy carbonyl, C₂-C₄ alkenyl optionally substituted with C₁-C₄ alkoxy carbonyl, C₂-C₄ alkynyl, or carboxaldehyde.

Embodiment A17. Compounds according to embodiment A16, wherein

30 R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇,

(C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-.

Embodiment A18. Compounds according to embodiment
5 A17, wherein

R₄ is H, or (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, OH, or -NR₆R₇.

10

Embodiment A19. Compounds according to embodiment A18, wherein

R₅ is phenyl, naphthyl, indolyl, pyridyl, quinolinyl, isoquinolinyl, isoindolyl, indol-2-onyl, indolyl(C₁-C₆)
15 alkyl, quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, pyridazinyl, pyrimidinyl, or pyrazinyl, pyridazinyl(C₁-C₆) alkyl, pyrimidinyl(C₁-C₆) alkyl, or pyrazinyl(C₁-C₆) alkyl, each of which is unsubstituted or substituted with 1, 2,
20 3, 4 or 5 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -NR₈R₉, -C(O)NR₆R₇, NR₆R₇ C₁-C₄ alkyl, and amidinoxime; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄
25 alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl C₁-C₄ alkyl, phenyl C₁-C₄ alkoxy, or phenyl C₁-C₄ alkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, hydroxy, C₁-
30 C₄ alkoxy, C₁-C₄ alkyl, OH, SH, C₃-C₆ cycloalkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring

which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A20. Compounds according to embodiment A19, wherein

R₁ is H, halogen, methyl, ethyl, C₂-C₄ alkenyl C₂-C₄ alkynyl, or carboxaldehyde;

R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, NR₆R₇ C₁-C₄ alkyl, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, or pyridyl; and

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, OH, or -NR₆R₇.

Embodiment A21. Compounds according to embodiment A20, wherein

R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, -NR₁₀R₁₁, C₁-C₄ alkoxy, -C(O)NR₁₀R₁₁, -CO₂H, NR₁₀R₁₁ C₁-C₄ alkyl, C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkoxy, CHO, -SO₂NH₂, C₁-C₄ haloalkyl, C₁-C₆ hydroxyalkyl, -C₁-C₄ alkyl-NR₁₂C(O)NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)OR₁₅, or -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-R₁₅, wherein

R₁₀ and R₁₁ at each occurrence are independently H, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, OH, -SO₂ (C₁-C₆ alkyl), or C₁-C₆ alkanoyl, or

R₁₀, R₁₁, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl or halogen,

R₁₂ is H or C₁-C₆ alkyl;

R₁₃ and R₁₄ are independently H or C₁-C₆ alkyl; or

R₁₃ and R₁₄ and the nitrogen to which they are attached form a morpholinyl ring; and

R₁₅ is C₁-C₆ alkoxy; -OC(O)C₁-C₆ alkyl, OH.

Embodiment A22. Compounds according to embodiment A21, wherein

R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, -NR₁₀R₁₁, NR₁₀R₁₁ C₁-C₆ alkyl, C₁-C₄ alkoxy, or -C(O)NR₁₀R₁₁, -CO₂H, -C₁-C₄ alkyl-NR₁₀R₁₁, C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkoxy, CHO, -SO₂NH₂, C₁-C₄ haloalkyl, C₁-C₆ hydroxyalkyl, -C₁-C₄ alkyl-NR₁₂C(O)NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)OR₁₅, or -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-R₁₅ wherein

R₁₀ and R₁₁ at each occurrence are independently H, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, OH, -SO₂ (C₁-C₆ alkyl), or C₁-C₆ alkanoyl,

R₁₂ is H or C₁-C₆ alkyl;

R₁₃ and R₁₄ are independently H or C₁-C₆ alkyl; or

R₁₃ and R₁₄ and the nitrogen to which they are attached form a morpholinyl ring; and

R₁₅ is C₁-C₆ alkoxy; -OC(O)C₁-C₆ alkyl, OH.

Embodiment A23. Compounds according to embodiment A22, wherein

R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, -NR₁₀R₁₁, C₁-C₄ alkyl, C₁-C₄ alkoxy, -C(O)NR₁₀R₁₁, wherein

R₁₀ and R₁₁ at each occurrence are independently H, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, OH, -SO₂ (C₁-C₆ alkyl), C₁-C₆ alkanoyl.

Embodiment A24. Compounds according to embodiment A23, wherein

R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, -NR₁₀R₁₁, or C₁-C₄ alkoxy.

Embodiment A25. Compounds according to embodiment A23, wherein

R₅ is substituted with at least one -C(O)NR₁₀R₁₁.

Embodiment A26. Compounds according to embodiment A25, wherein

R₁₀ and R₁₁ at each occurrence are independently H, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl.

Embodiment 27. Compounds according to embodiment A26, wherein

R₁₀ is H.

Embodiment A28. Compounds according to embodiment A25, wherein

R₁₀ and R₁₁ at each occurrence are independently H, C₁-C₆ alkyl, OH, -SO₂ (C₁-C₆ alkyl), C₁-C₆ alkanoyl.

5

Embodiment A29. Compounds according to embodiment A20, wherein

R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, NH₂,
10 NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), C₁-C₄ alkoxy, -C(O)NR₁₀R₁₁, wherein each of the above alkyl groups is optionally substituted with 1 or 2 groups that are independently OH, or methoxy; wherein

15 R₁₀, R₁₁, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl or halogen.

Embodiment A30. Compounds according to embodiment A20, wherein

20 R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, C₁-C₄ alkoxy, -CO₂H, -C₁-C₄ alkyl-NR₁₀R₁₁, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkoxy, CHO, -SO₂NH₂, C₁-C₄ haloalkyl, C₁-C₆ hydroxyalkyl, -C₁-C₄ alkyl-NR₁₂C(O)NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)OR₁₅, or
25 -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-R₁₅, -OC(O)C₁-C₆ alkyl, or OH wherein

R₁₂ is H or C₁-C₆ alkyl;
30 R₁₃ and R₁₄ are independently H or C₁-C₆ alkyl; or R₁₃ and R₁₄ and the nitrogen to which they are attached form a morpholinyl ring;
R₁₅ is C₁-C₆ alkoxy.

Embodiment A31. Compounds according to embodiment A30, wherein

5 R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, -CO₂H, C₁-C₄ alkoxy, -CO₂H, C₁-C₄ alkoxy, CHO, -SO₂NH₂, C₁-C₄ haloalkyl, C₁-C₄ hydroxyalkyl.

Embodiment A32. Compounds according to embodiment A30, wherein

10 R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, -CO₂H, -C₁-C₄ alkyl-NR₁₀R₁₁, -C₁-C₄ alkyl-NR₁₂C(O)NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)OR₁₅, or -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-R₁₅, or -OC(O)C₁-C₆ alkyl, wherein

R₁₂ is H or C₁-C₆ alkyl;

R₁₃ and R₁₄ are independently H or C₁-C₆ alkyl; or

20 R₁₃ and R₁₄ and the nitrogen to which they are attached form a morpholinyl ring;

R₁₅ is C₁-C₆ alkoxy.

Embodiment A33. Compounds according to embodiment A31, wherein

25 R₅ is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, -CO₂H, -C₁-C₄ alkyl-NR₁₀R₁₁, -C₁-C₄ alkyl-NR₁₂C(O)NR₁₃R₁₄, -C₁-C₄ alkyl-NR₁₂C(O)-(C₁-C₄ alkyl)-NR₁₃R₁₄, wherein

30 R₁₂ is H or C₁-C₆ alkyl;

R₁₃ and R₁₄ are independently H or C₁-C₆ alkyl; or

R₁₃ and R₁₄ and the nitrogen to which they are attached form a morpholinyl ring.

Embodiment A34. Compounds according to any one of embodiments A30, A31, A32, or A33, wherein the phenyl group is substituted with two groups that are meta to each other.

5

Embodiment A35. Compounds according to any one of embodiments A30, A31, A32, or A33, wherein the phenyl group is substituted with two groups that are para to each other.

10 Embodiment A36. Compounds according to embodiment A20, wherein

R_5 is indolyl, pyridyl, pyridazinyl, pyrimidinyl, indazolyl, quinolinyl, isoquinolinyl, isoindolyl, indol-2-onyl, pyridazinyl, pyrimidinyl, or pyrazinyl, , each of which
15 is unsubstituted or substituted with 1, 2, 3, 4 or 5 groups that are independently C_1 - C_4 alkyl, halogen, CF_3 , OCF_3 , $-CO_2CH_3$, C_1 - C_4 hydroxyalkyl, C_1 - C_4 alkoxy, $-CO_2(C_1$ - C_5 alkyl), benzyloxy, NR_8R_9 , NR_6R_7 , C_1 - C_4 alkyl, $-C(O)NR_6R_7$, or amidinooxime; wherein

20 R_6 and R_7 are independently at each occurrence H, C_1 - C_4 alkyl, C_1 - C_4 hydroxyalkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy C_1 - C_4 alkyl, C_1 - C_4 alkanoyl, phenyl C_1 - C_4 alkyl, phenyl C_1 - C_4 alkoxy, or phenyl C_1 - C_4 alkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3
25 groups that are independently, halogen, OH, SH, C_3 - C_6 cycloalkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkyl, OH, CF_3 , or OCF_3 ; or

R_6 , R_7 , and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring
30 which is optionally substituted with 1 or 2 groups that are independently C_1 - C_4 alkyl, hydroxy, hydroxy C_1 - C_4 alkyl, or halogen.

Embodiment A38. Compounds according to embodiment A36, wherein

R₅ is indolyl, pyridyl, pyrimidinyl, indazolyl, or pyrazinyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -C(O)NR₆R₇, -NR₈R₉, NR₆R₇ C₁-C₄ alkyl, and amidinooxime; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl C₁-C₄ alkyl, phenyl C₁-C₄ alkoxy, or phenyl C₁-C₄ alkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

Embodiment A39. Compounds according to embodiment A38, wherein

R₅ is indolyl, pyridyl, or pyrazinyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups that are independently C₁-C₄ alkyl, halogen, CF₃, OCF₃, -CO₂CH₃, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, -CO₂(C₁-C₅ alkyl), benzyloxy, -C(O)NR₆R₇, NR₈R₉, NR₆R₇-C₁-C₄ alkyl-, and amidinooxime; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

Embodiment A40. Compounds according to embodiment A36, wherein

R_5 is indolyl, pyridyl, pyridazinyl, pyrimidinyl, or pyrazinyl, each of which is unsubstituted or substituted with 1, 2, 3, 4 or 5 groups that are independently C_1 - C_4 alkyl, halogen, CF_3 , OCF_3 , $-CO_2CH_3$, C_1 - C_4 hydroxyalkyl, C_1 - C_4 alkoxy, $-CO_2(C_1$ - C_5 alkyl), benzyloxy, $-C(O)NH_2$, $-C(O)NH(C_1$ - C_6 alkyl) wherein the alkyl group is optionally substituted with OH or methoxy, $-C(O)N(C_1$ - C_6 alkyl) wherein each alkyl group is independently and optionally substituted with OH or methoxy, $-C(O)NR_6R_7$, NR_8R_9 , NR_6R_7 C_1 - C_4 alkyl, $-C_1$ - C_4 alkyl- NH_2 , $-C_1$ - C_4 alkyl- $NH(C_1$ - C_6 alkyl) wherein each alkyl group is independently and optionally substituted with OH or methoxy, $-C_1$ - C_4 alkyl- $N(C_1$ - C_6 alkyl)(C_1 - C_6 alkyl) wherein each alkyl group is independently and optionally substituted with OH or methoxy, and amidinoxime; wherein

R_6 , R_7 , and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C_1 - C_4 alkyl, hydroxy, hydroxy C_1 - C_4 alkyl, or halogen.

Embodiment A42. Compounds according to any one of embodiments A37, A38, A39, or A40, , wherein

R_1 is H, halogen, methyl, or carboxaldehyde;

R_2 is benzyloxy, phenyloxy, phenyloxy(C_1 - C_6)alkyl, or phenyl (C_1 - C_4) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, $-(C_1$ - C_6)alkyl- $N(R)-CO_2R_{30}$, NR_6R_7 , (C_1 - C_4) haloalkyl, (C_1 - C_4) haloalkoxy, (C_1 - C_6) alkyl, $NR_6R_7(C_1$ - C_6)alkyl, pyridyl, morpholinyl, thiomorpholinyl, piperazinyl pyridyl(C_1 - C_6)alkyl, morpholinyl(C_1 - C_6)alkyl,

thiomorpholinyl(C₁-C₆)alkyl, or piperazinyl(C₁-C₆)alkyl
wherein the pyridyl, morpholinyl, thiomorpholinyl, and
piperazinyl rings are optionally substituted with 1 or 2
groups that are independently C₁-C₄ alkyl, or halogen;
5 wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄
alkyl optionally substituted with 1 or two groups
that are independently OH, halogen or methoxy, C₁-C₄
hydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl,
10 C₁-C₄ alkanoyl, benzyl, benzyloxy, or phenyl C₁-C₄
alkanoyl, wherein each is unsubstituted or
substituted with 1, 2, or 3 groups that are
independently, halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-
C₄ alkoxy, C₁-C₄ alkyl, CF₃, or OCF₃, and

15 R₄ is H, (C₁-C₃) alkyl optionally substituted with one or two
groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR,
-N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, -NR₆R₇, NR₆R₇C₁-C₄
alkyl, or hydroxy(C₁-C₃)alkyl.

20 Embodiment A43. Compounds according to embodiment
A42, wherein
R₁ is H or halogen.

Embodiment A44. Compounds according to embodiment
25 A18, wherein

R₅ is phenyl(C₁-C₆)alkyl, (C₁-C₆)alkyl, piperidinyl(C₁-C₆) alkyl,
thienyl(C₁-C₆) alkyl, indolyl (C₁-C₆) alkyl, naphthyl(C₁-
C₆)alkyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-C₆)alkyl,
quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl,
30 isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl,
pyridazinyl(C₁-C₆) alkyl, pyrazinyl(C₁-C₆) alkyl, or
pyrazinyl(C₁-C₆)alkyl, wherein

each of the above is unsubstituted or substituted with 1,
2, 3, 4, or 5 groups that are independently alkyl,
halogen, alkoxy, benzyloxy, hydroxyalkyl,
thioalkoxy, $-\text{CO}_2(\text{C}_1\text{-C}_5 \text{ alkyl})$, CO_2H , CN, amidinoxime,
5 NR_8R_9 , $\text{NR}_6\text{R}_7\text{-(C}_1\text{-C}_6 \text{ alkyl)-}$, $-\text{C(O)NR}_6\text{R}_7$, amidino, CF_3 ,
or OCF_3 ;

R_8 is hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkanoyl, phenyl
 $\text{C}_1\text{-C}_6$ alkyl and phenyl $\text{C}_1\text{-C}_6$ alkanoyl; and

R_9 is aminoalkyl, mono $\text{C}_1\text{-C}_6$ alkylamino $\text{C}_1\text{-C}_6$ alkyl, di $\text{C}_1\text{-C}_6$
10 C_6 alkylamino $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkanoyl,
phenyl $\text{C}_1\text{-C}_4$ alkyl, indazolyl, and phenyl $\text{C}_1\text{-C}_4$
alkanoyl.

In this embodiment, it is preferred that when R_2 is
benzyloxy, R_4 is H, and R_5 is benzyl or methyl, R_1 is not
15 hydrogen; and

no more than two of R_1 , R_2 , R_4 , and R_5 are simultaneously
hydrogen.

Embodiment A45. Compounds according to embodiment
20 A44, wherein

R_5 is phenyl($\text{C}_1\text{-C}_6$)alkyl, which is unsubstituted or substituted
with 1, 2, 3, 4, or 5 groups that are independently
alkyl, halogen, alkoxy, benzyloxy, thioalkoxy, $-\text{CO}_2(\text{C}_1\text{-C}_5$
alkyl), CO_2H , CN, amidinoxime, NR_8R_9 , $\text{NR}_6\text{R}_7\text{-(C}_1\text{-C}_6 \text{ alkyl)-}$,
25 $-\text{C(O)NR}_6\text{R}_7$, amidino, CF_3 , or OCF_3 ; wherein

R_6 and R_7 are independently at each occurrence H, $\text{C}_1\text{-C}_4$
alkyl, $\text{C}_1\text{-C}_4$ hydroxyalkyl, $\text{C}_1\text{-C}_4$ alkoxy, $\text{C}_1\text{-C}_4$ alkoxy
 $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkanoyl, phenyl $\text{C}_1\text{-C}_4$ alkyl,
phenyl $\text{C}_1\text{-C}_4$ alkoxy, or phenyl $\text{C}_1\text{-C}_4$ alkanoyl, wherein
30 each is unsubstituted or substituted with 1, 2, or 3
groups that are independently, halogen, OH, SH, $\text{C}_3\text{-C}_6$
cycloalkyl, $\text{C}_1\text{-C}_4$ alkoxy, $\text{C}_1\text{-C}_4$ alkyl, CF_3 , or OCF_3 ;
or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen;

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₆ alkyl and phenyl C₁-C₆ alkanoyl; and

R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl, di C₁-C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₄ alkyl, indazolyl, and phenyl C₁-C₄ alkanoyl.

Embodiment A46. Compounds according to embodiment A45, wherein

R₅ is phenyl(C₁-C₆)alkyl, which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently CN, halogen, C₁-C₄ alkoxy, C₁-C₄ thioalkoxy, C₁-C₄ haloalkyl, C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, -C(O)NR₂₀R₂₁, wherein

R₂₀ and R₂₁ are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, or

R₂₀, R₂₁, and the nitrogen to which they are attached form a piperazinyl, or morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl or halogen.

Embodiment A47. Compounds according to embodiment A46, wherein

R₅ is phenyl(C₁-C₄)alkyl, which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently CN, halogen, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ alkyl, C₁-C₄ haloalkoxy, -C(O)NR₂₀R₂₁, wherein

R₂₀ and R₂₁ are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, or

R₂₀, R₂₁, and the nitrogen to which they are attached form a piperazinyl, or morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl or halogen.

Embodiment A48. Compounds according to embodiment A47, wherein

R₅ is benzyl or phenethyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently CN, halogen, C₁-C₄ alkoxy, CF₃, OCF₃, C₁-C₄ alkyl, -C(O)NR₂₀R₂₁, wherein

R₂₀ and R₂₁ are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, or

R₂₀, R₂₁, and the nitrogen to which they are attached form a piperazinyl, or morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl or halogen.

Embodiment A49. Compounds according to embodiment A48, wherein

R₅ is benzyl or phenethyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, methoxy, ethoxy, CF₃, OCF₃, methyl, ethyl, or -C(O)NR₂₀R₂₁, wherein

R₂₀ and R₂₁ are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl,

Embodiment A50. Compounds according to embodiment A48, wherein

R₅ is benzyl or phenethyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are

independently halogen, methoxy, ethoxy, CF₃, OCF₃, methyl, ethyl, or -C(O)NR₂₀R₂₁, wherein

R₂₀, R₂₁, and the nitrogen to which they are attached form a piperazinyl, or morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl or halogen.

Embodiment A51. Compounds according to embodiment A49, wherein

R₅ is substituted on the phenyl ring with 1, 2, 3, 4, or 5 groups and wherein there is a group at the para position of the phenyl.

Embodiment A52. Compounds according to embodiment A43, wherein

R₅ is piperidinyl(C₁-C₆) alkyl, thienyl(C₁-C₆) alkyl, indolyl(C₁-C₆) alkyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-C₆)alkyl, quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, pyridazinyl(C₁-C₆) alkyl, or pyrazinyl(C₁-C₆) alkyl, or pyrazinyl(C₁-C₆)alkyl, or pyrazinyl(C₁-C₆)alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl, halogen, C₁-C₆ alkoxy, C₁-C₆ hydroxyalkyl, benzyloxy, C₁-C₆ thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂H, CN, amidinoxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, CF₃, or OCF₃;

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₆ alkyl and phenyl C₁-C₆ alkanoyl; and

R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl, di C₁-C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₄ alkyl, indazolyl, and phenyl C₁-C₄ alkanoyl.

In this embodiment, it is preferred that when R₂ is benzyloxy, R₄ is H, and R₅ is benzyl or methyl, R₁ is not hydrogen; and

no more than two of R₁, R₂, R₄, and R₅ are simultaneously
5 hydrogen.

Embodiment A53. Compounds according to embodiment A52, wherein

R₅ is piperidiny(C₁-C₄) alkyl, thienyl(C₁-C₄) alkyl, indolyl
10 (C₁-C₄) alkyl, pyridyl(C₁-C₄)alkyl, pyrimidyl(C₁-C₄)alkyl,
or pyrazinyl(C₁-C₄)alkyl, each of which is unsubstituted.

Embodiment A54. Compounds according to embodiment A52, wherein

15 R₅ is indolyl (C₁-C₄) alkyl, pyrimidyl(C₁-C₄)alkyl, or
pyrazinyl(C₁-C₄)alkyl, wherein
each of the above is unsubstituted or substituted with 1,
2, 3, or 4 groups that are independently C₁-C₆ alkyl,
halogen, C₁-C₆ alkoxy, C₁-C₆ hydroxyalkyl, benzyloxy,
20 C₁-C₆ thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂H, CN,
amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, amidino,
-C(O)NR₂₀R₂₁, CF₃, or OCF₃; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₄
alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy
25 C₁-C₄ alkyl, C₁-C₄ alkanoyl, benzyl, benzyloxy, or
phenyl C₁-C₄ alkanoyl, wherein each is unsubstituted
or substituted with 1, 2, or 3 groups that are
independently, halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-
C₄ alkoxy, C₁-C₄ alkyl, CF₃, or OCF₃; or

30 R₆, R₇, and the nitrogen to which they are attached form a
morpholinyl, thiomorpholinyl, or piperazinyl ring
which is optionally substituted with 1 or 2 groups

that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen;

R₈ is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₄ alkyl and phenyl C₁-C₄ alkanoyl; and

R₉ is aminoalkyl, mono C₁-C₆ alkylamino C₁-C₆ alkyl, di C₁-C₆ alkylamino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl C₁-C₄ alkyl, indazolyl, and phenyl C₁-C₄ alkanoyl;

R₂₀ and R₂₁ are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, or

R₂₀, R₂₁, and the nitrogen to which they are attached form a piperazinyll, or morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl or halogen

Embodiment A55. Compounds according to embodiment A54, wherein

R₅ is indolyl (C₁-C₄) alkyl, or pyrazinyl(C₁-C₄)alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, or 4 groups that are independently C₁-C₆ alkyl, halogen, C₁-C₆ alkoxy, C₁-C₆ hydroxyalkyl, benzyloxy, C₁-C₆ thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂H, CN, -C(O)NR₂₀R₂₁, CF₃, or OCF₃; wherein

R₂₀ and R₂₁ are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, or

R₂₀, R₂₁, and the nitrogen to which they are attached form a piperazinyll, or morpholinyl ring, each of which is optionally substituted with 1 or 2 groups that are independently alkyl or halogen.

Embodiment A56. Compounds according to embodiment A52, wherein

R₅ is isoquinolinyl, isoindolyl, indol-2-onyl, quinolinyl(C₁-C₆) alkyl, isoquinolinyl(C₁-C₆) alkyl, isoindolyl(C₁-C₆) alkyl, indol-2-onyl(C₁-C₆) alkyl, wherein
 each of the above is unsubstituted or substituted with 1,
 5 2, 3, 4, or 5 groups that are independently C₁-C₆
 alkyl, halogen, C₁-C₆ alkoxy, C₁-C₆ hydroxyalkyl,
 benzyloxy, C₁-C₆ thioalkoxy, -CO₂(C₁-C₅ alkyl), CO₂H,
 CN, amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-,
 -C(O)NR₆R₇, amidino, CF₃, or OCF₃.

10

Embodiment A57. Compounds according to embodiment A1,
 wherein

R₁ is H, halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
 or carboxaldehyde;

15 R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or
 phenyl (C₁-C₄) thioalkoxy, wherein each of the above is
 optionally substituted with 1, 2, 3, or 4 groups that are
 independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇,
 (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl,
 20 pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two
 groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -
 N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, or
 hydroxy(C₁-C₄)alkyl;

25 R₅ is C₃-C₇ cycloalkyl or C₃-C₇ cycloalkylalkyl, each of which
 is optionally substituted with 1 or 2 groups that are
 independently alkyl, alkoxy, halogen, -NR₆R₇, or NR₆R₇-(C₁-
 C₆ alkyl)-, wherein each of the alkyl groups is optionally
 substituted with 1 or 2 groups that are independently OH,
 30 methoxy, NH₂, or halogen.

Embodiment A58. Compounds according to embodiment
 A57, wherein

R₅ is C₃-C₇ cycloalkyl or C₃-C₇ cycloalkyl C₁-C₄ alkyl, each of which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, halogen, -NR₆R₇, or NR₆R₇-(C₁-C₆ alkyl)- wherein each of the alkyl groups is optionally substituted with 1 or 2 groups that are independently OH, methoxy, or NH₂;

R₆ and R₇ are independently at each occurrence H, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy C₁-C₄ alkyl, C₁-C₄ alkanoyl, benzyl, benzyloxy, or phenyl C₁-C₄ alkanoyl, wherein each is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A59. Compounds according to embodiment A58, wherein

R₁ is H, halogen, methyl, ethyl;

R₂ is benzyloxy, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, amino, mono or dialkylamino, -NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, methyl, (C₁-C₄)alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇ or hydroxy(C₁-C₂)alkyl.

Embodiment A60. Compounds according to embodiment A59, wherein

R₂ is substituted with two halogens and is further optionally substituted with 1 or 2 groups that are independently
 5 halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, amino, mono or dialkylamino, -NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, or NR₆R₇-(C₁-C₆ alkyl).

Embodiment A61. Compounds according to embodiment A1,
 10 wherein

R₅ is H, alkyl optionally substituted with 1, 2, or 3 groups that are independently phenylalkoxycarbonyl, -NR₈R₉, halogen, -C(O)NR₈R₉, alkoxycarbonyl, or alkanoyl, alkoxyalkyl optionally substituted with one
 15 trimethylsilyl group, alkoxycarbonyl, amino, hydroxyalkyl, alkenyl optionally substituted with alkoxycarbonyl, alkynyl, -SO₂-alkyl, or alkoxy optionally substituted with one trimethylsilyl group, wherein

each of the above is unsubstituted or substituted with 1,

20 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, phenylalkoxy, thioalkoxy, -SO₂alkyl, alkoxycarbonyl, phenylalkoxycarbonyl, CO₂H, CN, OH, amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, hydroxyalkyl, carboxaldehyde, -NR₆R₇,
 25 haloalkyl, or haloalkoxy;

wherein R₈ is hydrogen, alkyl, alkanoyl, phenylalkyl and arylalkanoyl; and

wherein R₉ is alkyl, alkanoyl, phenylalkyl, heteroaryl, aminoalkyl, monoalkylaminoalkyl,
 30 dialkylaminoalkyl, and arylalkanoyl.

In this embodiment, it is preferred that when R₂ is benzyloxy, R₄ is H, and R₅ is benzyl or methyl, R₁ is not hydrogen; and

no more than two of R_1 , R_2 , R_4 , and R_5 are simultaneously hydrogen.

Embodiment A62. Compounds according to embodiment A1,
5 wherein

R_5 is H, alkyl optionally substituted with 1, 2, or 3 groups that are independently phenylalkoxycarbonyl, $-NR_8R_9$, halogen, $-C(O)NR_8R_9$, alkoxycarbonyl, or alkanoyl, alkoxyalkyl optionally substituted with one
10 trimethylsilyl group, alkoxycarbonyl, amino, hydroxyalkyl, alkenyl optionally substituted with alkoxycarbonyl, alkynyl, $-SO_2$ -alkyl, alkoxy optionally substituted with one trimethylsilyl group, wherein

each of the above is unsubstituted or substituted with 1,
15 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, phenylalkoxy, thioalkoxy, $-SO_2$ alkyl, alkoxycarbonyl, phenylalkoxycarbonyl, CO_2H , CN, OH, amidinooxime, NR_8R_9 , $NR_6R_7-(C_1-C_6 \text{ alkyl})-$, $-C(O)NR_6R_7$, amidino, hydroxyalkyl, carboxaldehyde, $-NR_6R_7$,
20 haloalkyl, or haloalkoxy;

wherein R_8 is hydrogen, alkyl, alkanoyl, phenylalkyl and arylalkanoyl; and

wherein R_9 is alkyl, alkanoyl, phenylalkyl, heteroaryl, aminoalkyl, monoalkylaminoalkyl,
25 dialkylaminoalkyl, and arylalkanoyl.

In this embodiment, it is preferred that when R_2 is benzyloxy, R_4 is H, and R_5 is benzyl or methyl, R_1 is not hydrogen; and

no more than two of R_1 , R_2 , R_4 , and R_5 are simultaneously
30 hydrogen.

Embodiment A63. Compounds according to embodiment A62, wherein

R₁ is H, halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, or carboxaldehyde;

R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, or hydroxy(C₁-C₄)alkyl.

Embodiment A64. Compounds according to embodiment A63, wherein

R₅ is H, alkyl optionally substituted with 1, 2, or 3 groups that are independently phenylalkoxycarbonyl, -NR₈R₉, halogen, -C(O)NR₈R₉, alkoxycarbonyl, or alkanoyl, alkoxyalkyl optionally substituted with one trimethylsilyl group, alkoxycarbonyl, amino, hydroxyalkyl, alkenyl optionally substituted with alkoxycarbonyl, alkynyl, -SO₂-alkyl, alkoxy optionally substituted with one trimethylsilyl group, wherein

wherein R₈ is hydrogen, C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl C₁-C₄ alkyl and phenyl C₁-C₄ alkanoyl; wherein R₉ is C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl C₁-C₄ alkyl, pyridyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, and phenyl C₁-C₄ alkanoyl.

Embodiment A65. Compounds according to embodiment A64, wherein

R₅ is C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently phenyl C₁-C₄ alkoxycarbonyl, NH₂,

mono C₁-C₄ alkylamino, di C₁-C₄ alkylamino, halogen,
 -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) wherein the alkyl is
 optionally substituted with OH, NH₂, or methoxy, -C(O)N
 (C₁-C₆ alkyl) (C₁-C₆ alkyl) wherein each alkyl is
 5 optionally substituted with OH, NH₂, or methoxy, C₁-C₄
 alkoxy carbonyl, and C₁-C₄ alkanoyl, or

R₅ is C₁-C₄ alkoxy C₁-C₄ alkyl, C₁-C₄ alkoxy carbonyl, amino, C₁-
 C₄ hydroxyalkyl, C₂-C₄ alkenyl optionally substituted with
 C₁-C₄ alkoxy carbonyl, C₂-C₄ alkynyl, -SO₂- C₁-C₄ alkyl, or
 10 C₁-C₄ alkoxy.

Embodiment A66. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

15 R₁ is halogen, NO₂, alkyl, carboxaldehyde, hydroxyalkyl,
 arylalkoxy, arylalkyl, CN, aryl, alkanoyl, alkoxy,
 alkoxyalkyl, haloalkyl, or arylalkanoyl,

wherein the aryl portion of arylalkoxy, arylalkyl, and
 arylalkanoyl is unsubstituted or substituted with 1,
 20 2, 3, 4, or 5 groups that are independently halogen,
 (C₁-C₄)alkyl, (C₁-C₄) alkoxy, nitro, CN, haloalkyl,
 haloalkoxy or CO₂H;

wherein the alkyl portion of the alkyl, hydroxyalkyl,
 arylalkoxy, arylalkyl, alkanoyl, alkoxy, alkoxyalkyl
 25 and arylalkanoyl groups is unsubstituted or
 substituted with 1, 2, or 3 groups that are
 independently halogen, C₁-C₄ alkoxy, C₁-C₄
 alkoxy carbonyl, or spirocyclopropyl;

R₂ is aryl, heteroaryl, arylalkenyl, arylalkoxy, aryloxyalkyl,
 30 arylalkyl, OH, alkynyl, aryloxy, aryloxyalkyl,

arylthioalkoxy, alkoxy, $-OC(O)NH(CH_2)_n$ aryl,
 $-OC(O)N(alkyl)(CH_2)_n$ aryl, $-OSO_2(C_1-C_6)alkyl$, $-OSO_2aryl$,
 alkyl, alkoxyalkoxy, NR_8R_9 , or CO_2H , wherein
 n is 0, 1, 2, 3, 4, 5 or 6;

5 each of the above is unsubstituted or substituted with 1,
 2, 3, 4, or 5 groups that are independently halogen,
 $-(C_1-C_6)alkyl-N(R)-CO_2R_{30}$, alkoxy, alkoxycarbonyl, CN,
 NR_6R_7 , haloalkyl, haloalkoxy, alkyl, heteroaryl,
 heteroarylalkyl, $NR_6R_7-(C_1-C_6 alkyl)-$, phenyl, $-SO_2-$
 10 phenyl wherein the phenyl groups are optionally
 substituted with 1, 2, or 3 groups that are
 independently halogen or NO_2 ; or $-OC(O)NR_6R_7$, wherein
 R_6 and R_7 are independently at each occurrence H,
 alkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, -
 15 $SO_2-alkyl$, OH, hydroxyalkyl, $-(C_1-C_4)alkyl-CO_2-$
 $alkyl$, heteroarylalkyl, alkanoyl, arylalkyl,
 arylalkoxy, or arylalkanoyl, wherein each of
 the above is unsubstituted or substituted with
 1, 2, or 3 groups that are independently,
 20 halogen, alkoxy, heterocycloalkyl, OH, SH, C_3-C_6
 cycloalkyl, NH_2 , $NH(alkyl)$, $N(alkyl)(alkyl)$, $-O-$
 alkanoyl, alkyl, haloalkyl, or haloalkoxy; or
 R_6 , R_7 , and the nitrogen to which they are attached
 form a morpholinyl, thiomorpholinyl,
 25 piperidinyl, pyrrolidinyl, or piperazinyl ring
 which is optionally substituted with 1 or 2
 groups that are independently $C_1-C_4 alkyl$, C_1-C_4
 alkoxy, hydroxy, hydroxy $C_1-C_4 alkyl$, or
 halogen;

30 R at each occurrence is independently H or C_1-C_6
 alkyl;

R_{30} is $C_1-C_6 alkyl$ optionally substituted with 1 or 2
 groups that are independently OH, SH, halogen,

amino, monoalkylamino, dialkylamino or C₃-C₆ cycloalkyl;

R₄ is H, alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, arylalkoxy, arylalkyl, hydroxyalkyl, haloalkyl, alkoxy, carboxaldehyde, CO₂H, alkoxyalkyl, or alkoxyalkoxy, wherein

the aryl portion of arylalkoxy, arylalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy; and

R₅ is H, arylalkyl, alkyl, aryl, alkoxy, heterocycloalkylalkyl, heteroarylalkyl, heterocycloalkyl, cycloalkyl, cycloalkylalkyl, -alkyl-S-aryl, -alkyl-SO₂-aryl, -(C₁-C₄)alkyl-C(O)-heterocycloalkyl, -SO₂-aryl, or heteroaryl, wherein

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, aryl, arylalkoxy, thioalkoxy, alkoxycarbonyl, arylalkoxycarbonyl, OH, CO₂H, CN, amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, amidino, hydroxyalkyl, -SO₂alkyl, -SO₂H, -SO₂NR₆R₇, -NR₆R₇, alkanoyl wherein the alkyl portion is optionally substituted with OH, halogen or alkoxy, haloalkyl, -(C₁-C₄ alkyl)-NR₁₅C(O)NR₁₆R₁₇, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, -O-CH₂-O-, -O-CH₂CH₂-O-, or haloalkoxy; wherein

R₈ at each occurrence is independently hydrogen, alkyl, alkanoyl, arylalkyl and arylalkanoyl wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that

are independently alkyl, alkoxy, alkoxy carbonyl, halogen, or haloalkyl; and
R₉ at each occurrence is independently alkyl, alkanoyl, arylalkyl, cycloalkyl, alkenyl, heteroaryl, cycloalkylalkyl, arylalkanoyl, -SO₂-phenyl, and aryl wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, alkoxy, alkoxy carbonyl, halogen, or haloalkyl;

10 R₁₅ is H or C₁-C₆ alkyl;
R₁₆ and R₁₇ are independently H or C₁-C₆ alkyl; or
R₁₆, R₁₇, and the nitrogen to which they are attached form a morpholinyl ring; and
R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that:

R₆ and R₇ are not simultaneously OH;
20 R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl);
when R₂ is OH, R₄ is methyl and R₅ is phenyl, R₁ is not acetyl;
and
R₄ and R₅ are not simultaneously hydrogen.

25 Embodiment A71. Compounds according to
embodiment A66 wherein
R₁ is halogen, C₁-C₆ alkyl, phenyl, carboxaldehyde, C₁-C₆ hydroxyalkyl, phenyl C₁-C₆ alkoxy, phenyl C₁-C₆ alkyl, CN, C₁-C₆ alkanoyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ haloalkyl, or phenyl C₁-C₆ alkanoyl,
30 wherein the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are

independently halogen, (C₁-C₄)alkyl, (C₁-C₄) alkoxy, nitro, CN, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy or CO₂H; wherein the above alkyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy,

R₂ is phenylalkoxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, phenylthio(C₁-C₄)alkoxy, alkoxy, alkenyl, phenethyl, -OC(O)NH(CH₂)_nphenyl, -OC(O)N(alkyl)(CH₂)_nphenyl, alkyl, alkoxyalkoxy, NR₈R₉, pyridyl, pyrimidyl, pyridazyl, pyrazolyl, imidazolyl, pyrrolyl, tetrahydroquinolinyl, amino, tetrahydroisoquinolinyl, tetrazolyl, pyrazinyl, benzimidazolyl, triazinyl, tetrahydrofuryl, piperidinyl, hexahydropyrimidinyl, thiazolyl, thienyl, or CO₂H, wherein n is 0, 1, 2, or 3;

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, haloalkyl, haloalkoxy, alkyl, thienyl, pyridyl, or phenyl optionally substituted with 1, 2, or 3 halogens;

R₆ and R₇ are independently at each occurrence H, alkyl, alkoxy, alkoxyalkyl, hydroxyalkyl, alkoxycarbonyl, -(C₁-C₄)alkyl-CO₂-alkyl, alkanoyl, phenylalkyl, phenylalkoxy, or phenylalkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, SH, C₃-C₆ cycloalkyl, alkoxy, NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), alkyl, CF₃ or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen;

R₄ is H, alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenylalkoxy, phenylalkyl, hydroxyalkyl, carboxaldehyde, haloalkyl, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy; and

R₅ is benzyl, phenethyl, (C₁-C₆)alkyl, phenyl, naphthyl, alkoxy, piperidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, isoquinolinyl, tetrahydroisoquinolinyl, indolyl, 1H-indazolyl, pyridyl, pyrimidyl, pyridazyl, pyrazinyl, piperidinyl(C₁-C₆)alkyl, pyrrolidinyl(C₁-C₆)alkyl, imidazolidinyl(C₁-C₆)alkyl, piperazinyl(C₁-C₆)alkyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-C₆)alkyl, pyridazyl(C₁-C₆)alkyl, pyrazinyl(C₁-C₆)alkyl, isoquinolinyl(C₁-C₆)alkyl, tetrahydroisoquinolinyl(C₁-C₆)alkyl, indolyl(C₁-C₆)alkyl, or 1H-indazolyl(C₁-C₆)alkyl, and wherein

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, hydroxyalkyl, phenylalkoxy, thioalkoxy, alkoxycarbonyl, phenylalkoxycarbonyl, OH, CO₂H, CN, amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, piperazinyl, morpholinyl, -SO₂(C₁-C₆) alkyl, -SO₂NH₂, -SO₂NH(C₁-C₆)alkyl, -SO₂N(C₁-C₆)alkyl (C₁-C₆)alkyl, haloalkyl, or haloalkoxy.

In this embodiment, it is preferred that when R₂ is OH, R₄ is methyl and R₅ is phenyl, R₁ is not acetyl; and R₄ and R₅ are not simultaneously hydrogen.

Embodiment A72. Compounds according to embodiment A71 wherein

R₁ is halogen, alkyl, carboxaldehyde, hydroxyalkyl, phenylalkoxy, phenyl, benzyl, phenethyl, phenpropyl, phenbutyl, CN, (C₂-C₆)alkanoyl, haloalkyl, or phenylCO-,
5 phenylCH₂CO-, phenylCH₂CH₂CO-,

wherein the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, (C₁-C₄)alkyl, (C₁-C₄) alkoxy,
10 nitro, CN, haloalkyl, haloalkoxy or CO₂H;

wherein the above alkyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy,

R₂ is benzyloxy, phenethyloxy, phenpropyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, phenylthio(C₁-C₄)alkoxy, NR₈R₉, (C₁-C₆)alkyl, alkynyl, phenethyl, -OC(O)N(CH₃)CH₂phenyl, alkoxyalkoxy, pyridyl, pyrimidyl, pyridazyl, pyrazolyl, imidazolyl, pyrrolyl, pyrazinyl, piperidinyl, hexahydropyrimidinyl, benzimidazolyl, or thienyl, wherein
15 each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, CF₃, OCF₃, (C₁-C₄)alkyl, thienyl, pyridyl, or phenyl optionally substituted with 1, 2, or 3 halogens;

R₆ and R₇ are independently at each occurrence H, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl, hydroxy(C₁-C₆)alkyl, -(C₁-C₄)alkyl-CO₂-alkyl, (C₁-C₆)alkanoyl, phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy, or phenyl(C₁-C₆)alkanoyl, wherein each of the above is
25 unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, (C₁-C₆)alkoxy, NH₂,

OH, SH, C₃-C₆ cycloalkyl, (C₁-C₆)alkyl, CF₃ or OCF₃;
or

R₆, R₇, and the nitrogen to which they are attached form a
morpholinyl, piperidinyl, pyrrolidinyl, or
5 piperazinyl ring which is optionally substituted
with 1 or 2 groups that are independently C₁-C₄
alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen;

R₄ is H, alkyl optionally substituted with one or two groups
that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -
10 N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇,
benzyloxy, phenethyloxy, phenpropyloxy, benzyl,
phenethyl, phenpropyl, hydroxyalkyl, halo(C₁-C₄)alkyl,
carboxaldehyde, alkoxy, alkoxyalkyl, or alkoxyalkoxy,
wherein

15 the above phenyl groups are unsubstituted or substituted
with 1, 2, or 3 groups that are independently
halogen, hydroxy, alkoxy, alkyl, nitro, CF₃ or OCF₃;
and

R₅ is benzyl, phenethyl, phenpropyl, phenbutyl, (C₁-C₆)alkyl,
20 phenyl, piperidinyl, pyrrolidinyl, imidazolidinyl,
piperidinyl(C₁-C₆)alkyl, pyrrolidinyl(C₁-C₆)alkyl,
imidazolidinyl(C₁-C₆)alkyl, pyridyl, pyrimidyl, pyridazyl,
pyrazinyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-C₆)alkyl,
pyridazyl(C₁-C₆)alkyl, or pyrazinyl(C₁-C₆)alkyl wherein

25 each of the above is unsubstituted or substituted with 1,
2, 3, 4, or 5 groups that are independently alkyl,
halogen, haloalkyl, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-,
carboxaldehyde, morpholinyl, SO₂NH₂, SO₂NH(alkyl),
SO₂N(alkyl)(alkyl), alkoxy, hydroxyalkyl, benzyloxy,
30 thioalkoxy, OH, CO₂H, CN, -CO₂(C₁-C₅ alkyl),
phenylalkoxycarbonyl, amidinoxime, amidino,
-C(O)NR₆R₇, CF₃, CF₂CF₃, ClCH₂, or OCF₃.

In this embodiment, it is preferred that when R_2 is OH, R_4 is methyl and R_5 is phenyl, R_1 is not acetyl.

Embodiment A73. Compounds according to embodiment A72
5 wherein

R_1 is halogen, alkyl, carboxaldehyde, hydroxy(C_1 - C_4)alkyl, phenylalkoxy, benzyl, phenethyl, $-C(O)CH_3$, phenylCO-, or phenylCH₂CO-,

10 wherein the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, (C_1 - C_4)alkyl, (C_1 - C_4)alkoxy, nitro, CN, CF₃, or OCF₃;

15 wherein the above alkyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy;

R_2 is benzyloxy, phenethyloxy, phenpropyloxy, OH, phenyloxy, phenyloxy(C_1 - C_6)alkyl, phenethyl, NR₈R₉, -S-benzyl, or (C_1 - C_6)alkyl, wherein

20 each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, $-(C_1-C_6)alkyl-N(R)-CO_2R_{30}$, CF₃, OCF₃, alkyl, thienyl, or pyridyl;

25 R_6 and R_7 are independently at each occurrence H, (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, (C_1 - C_6)alkoxy(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonyl, hydroxy(C_1 - C_6)alkyl, $-(C_1-C_4)alkyl-CO_2-alkyl$, (C_1 - C_6)alkanoyl, phenyl(C_1 - C_6)alkyl, phenyl(C_1 - C_6)alkoxy, or phenyl(C_1 - C_6)alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups
30 that are independently, halogen, (C_1 - C_6)alkoxy, NH₂, OH, SH, C_3 - C_6 cycloalkyl, (C_1 - C_6)alkyl, CF₃ or OCF₃;
or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen;

R₄ is H, alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, benzyloxy, phenethyloxy, phenpropyloxy, benzyl, or hydroxyalkyl, wherein

the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, CF₃ or OCF₃; and

R₅ is benzyl, phenethyl, phenpropyl, phenbutyl, (C₁-C₆)alkyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, pyrazinyl(C₁-C₆)alkyl, pyrimidinyl(C₁-C₆)alkyl, or pyridyl(C₁-C₄)alkyl, wherein

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, haloalkyl, morpholinyl, -SO₂ (C₁-C₆) alkyl, -SO₂NH₂, -SO₂NH(C₁-C₆), -SO₂N(C₁-C₆)(C₁-C₆), (C₁-C₄)alkoxy, phenyl(C₁-C₄)alkoxy, thio(C₁-C₄)alkoxy, (C₁-C₄)alkoxycarbonyl, OH, CO₂H, CN, amidinooxime, amidino, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, hydroxyalkyl, CONR₆R₇, CF₃, or OCF₃.

Embodiment A74. Compounds according to embodiment A73 wherein

R₁ is halogen, alkyl, carboxaldehyde, or hydroxyalkyl;

R₂ is benzyloxy, phenethyloxy, phenpropyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, phenethyl, phenylthioalkoxy, or (C₁-C₆)alkyl, wherein

each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, $-(C_1-C_6)alkyl-N(R)-CO_2R_{30}$, CF_3 , OCF_3 , alkyl, thienyl, or pyridyl;

5 R_4 is H, (C_1-C_4) alkyl optionally substituted with one or two groups that are independently CO_2H , $-CO_2alkyl$, $-C(O)NRR$, $-N(R_{30})C(O)NRR$, $-N(R_{30})C(O)-(C_1-C_6)alkoxy$, or $-NR_6R_7$, benzyloxy, or phenethyloxy, wherein the above phenyl groups are unsubstituted or substituted
10 with 1, 2, or 3 groups that are independently halogen, hydroxy, $(C_1-C_4)alkoxy$, $(C_1-C_4)alkyl$, nitro, CF_3 or OCF_3 ; and

R_5 is benzyl, phenethyl, $(C_1-C_6)alkyl$, phenyl, indazolyl, or pyridyl, wherein each of the above is unsubstituted or
15 substituted with 1, 2, 3, 4, or 5 groups that are independently $(C_1-C_4)alkyl$, halogen, OH, CO_2H , CN, $(C_1-C_4)alkoxy$, $-C(O)pyrrolidine$, $-SO_2(C_1-C_6)alkyl$, benzyloxy, $-CO_2(C_1-C_5)alkyl$, amidino, thio $(C_1-C_4)alkoxy$, amidinooxime, CF_3 , NR_8R_9 , $NR_6R_7-(C_1-C_6)alkyl-$, $CONR_6R_7$, or
20 OCF_3 .

Embodiment A75. Compounds according to embodiment A74 wherein

R_1 is chloro, bromo, iodo, methyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl;
25 and

R_5 is benzyl, phenethyl, phenpropyl, phenyl, or pyridyl, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently alkyl, OH, halogen, alkoxy, NH_2 , $NH(C_1-C_6)alkyl$, $N(C_1-C_6)alkyl(C_1-C_6)alkyl$, NR_8R_9 , $NR_6R_7-(C_1-C_6)alkyl-$, $CONR_6R_7$, and amidinooxime; wherein
30 R_6 and R_7 are independently H, C_1-C_4 alkyl, C_1-C_6 alkanoyl, wherein the alkyl and alkanoyl groups are optionally

substituted with 1, 2, or 3 groups that are independently OH, halogen, or C₃-C₇ cyclopropyl.

Embodiment A76. Compounds according to embodiment A75

5 wherein

R₂ is benzyloxy, phenethyl, phenyloxy(C₁-C₆)alkyl, or phenethyloxy, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, CF₃, OCF₃, or (C₁-C₄)alkyl.

10

Embodiment A77. Compounds according to embodiment A66, wherein

R₅ is benzyl, phenethyl, thienyl(C₁-C₆ alkyl), piperidinyl(C₁-C₆)alkyl, pyrrolidinyl(C₁-C₆)alkyl, imidazolidinyl(C₁-C₆)alkyl, piperazinyl(C₁-C₆)alkyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-C₆)alkyl, pyridazyl(C₁-C₆)alkyl, pyrazinyl(C₁-C₆)alkyl, isoquinolinyl(C₁-C₆)alkyl, tetrahydroisoquinolinyl(C₁-C₆)alkyl, indolyl(C₁-C₆)alkyl, or 1H-indazolyl(C₁-C₆)alkyl, wherein

15 each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently (C₁-C₆)alkyl, halogen, (C₁-C₆)alkoxy, (C₁-C₆)hydroxyalkyl, phenyl(C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, (C₁-C₆)alkoxycarbonyl, phenyl(C₁-C₆)alkoxycarbonyl, OH, CO₂H, CN, amidinoxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, piperazinyl, morpholinyl, -SO₂(C₁-C₆)alkyl, -SO₂NH₂, -SO₂NH(C₁-C₆)alkyl, -SO₂N(C₁-C₆)alkyl (C₁-C₆)alkyl, (C₁-C₄)haloalkyl, -(C₁-C₄alkyl)-NR₁₅C(O)NR₁₆R₁₇, -(C₁-C₄alkyl)-NR₁₅C(O)R₁₈, -O-CH₂-O, -O-CH₂CH₂-O-, or (C₁-C₄)haloalkoxy; wherein

20 R₆ and R₇ are independently at each occurrence H, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-

25

30

C₆)alkyl, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)hydroxyalkyl, -(C₁-C₄)alkyl-CO₂-(C₁-C₆)alkyl, (C₁-C₆)alkanoyl, phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy, or phenyl(C₁-C₆)alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, (C₁-C₄)alkoxy, NH₂, OH, SH, C₃-C₆ cycloalkyl, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), (C₁-C₄)alkyl, CF₃ or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen; and R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A78. Compounds according to embodiment A77, wherein R₁ is halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, or carboxaldehyde; R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇,

(C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, or pyridyl; and

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, or hydroxy(C₁-C₄)alkyl.

Embodiment A79. Compounds according to embodiment A78, wherein

R₅ is benzyl, or phenethyl, wherein each is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently (C₁-C₆)alkyl, halogen, (C₁-C₆)alkoxy, (C₁-C₆)hydroxyalkyl, phenyl(C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, (C₁-C₆)alkoxycarbonyl, phenyl(C₁-C₆)alkoxycarbonyl, OH, CO₂H, CN, amidinoxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇amidino, piperazinyl, morpholinyl, -SO₂ (C₁-C₆) alkyl, -SO₂NH₂, -SO₂NH(C₁-C₆)alkyl, -SO₂N(C₁-C₆)alkyl (C₁-C₆)alkyl, (C₁-C₄)haloalkyl, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, -O-CH₂-O-, -O-CH₂CH₂-O-, or (C₁-C₄)haloalkoxy; wherein

R₆ and R₇ are independently at each occurrence H, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)hydroxyalkyl, -(C₁-C₄)alkyl-CO₂-(C₁-C₆)alkyl, (C₁-C₆)alkanoyl, phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy, or phenyl(C₁-C₆)alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, (C₁-C₄)alkoxy, NH₂, OH, SH, C₃-C₆ cycloalkyl, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), (C₁-C₄)alkyl, CF₃ or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is

optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen; and

R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, amino C₁-C₆ alkyl, or mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A80. Compounds according to embodiment A79, wherein

R₅ is benzyl or phenethyl, wherein each is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₈R₉, halogen, C₁-C₆ alkoxy, CO₂H, -(C₁-C₄ alkyl)-CO₂H, C₁-C₆ thioalkoxy, amidinooxime, C₁-C₆ alkoxycarbonyl, -(C₁-C₄ alkyl)-C₁-C₆ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, -(C₁-C₄ alkyl)-CN, CN, phenyl C₁-C₆ alkoxy, OH, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, NR₆R₇-(C₁-C₆ alkyl)-, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, amidinooxime, -SO₂(C₁-C₆ alkyl), -O-CH₂-O-, -O-CH₂CH₂-O-, phenyl C₁-C₄ alkoxy, or phenyl; wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl) each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃;

or

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl, thiomorpholinyl, ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen,

R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A81. Compounds according to embodiment A80, wherein

R₅ is benzyl or phenethyl, wherein each is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, halogen, C₁-C₆ alkoxy, CO₂H, -(C₁-C₄ alkyl)-CO₂H, C₁-C₆ thioalkoxy, amidinooxime, C₁-C₆ alkoxycarbonyl, -(C₁-C₄ alkyl)-C₁-C₆ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, -(C₁-C₄ alkyl)-CN, CN, phenyl C₁-C₆ alkoxy, OH, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, NR₆R₇-(C₁-C₆ alkyl)-, NR₈R₉, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, amidinooxime, -SO₂(C₁-C₆ alkyl), -O-CH₂-O-, -O-CH₂CH₂-O-, phenyl C₁-C₄ alkoxy, or phenyl; wherein R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl) each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆

cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃; and

R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A82. Compounds according to embodiment A81, wherein

R₅ is benzyl which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, halogen, C₁-C₄ alkoxy, CO₂H, C₁-C₄ thioalkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, CN, OH, NR₆R₇-(C₁-C₆ alkyl)-, NR₆R₉, -SO₂(C₁-C₆ alkyl), or benzyloxy; wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl) each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A83. Compounds according to embodiment A82, wherein

R₅ is benzyl which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, halogen, C₁-C₄ alkoxy, C₁-C₄ thioalkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, CN, NR₈R₉, or NR₆R₇-(C₁-C₆ alkyl)-; wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or C₁-C₄ alkoxy C₁-C₄ alkyl each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH.

Embodiment A84. Compounds according to embodiment A83, wherein

the R₅ group is disubstituted with two groups that are meta to each other.

Embodiment A86. Compounds according to embodiment A80, wherein

R₅ is benzyl which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, halogen, C₁-C₄ alkoxy, CO₂H, -(C₁-C₄ alkyl)-CO₂H, -(C₁-C₄ alkyl)-C₁-C₆ alkoxycarbonyl, -(C₁-C₄ alkyl)-CN, CN, phenyl C₁-C₆ alkoxy, CF₃, OCF₃, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, amidinooxime, -O-CH₂-O-, -O-CH₂CH₂-O-, or phenyl; wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₄ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₄ alkyl)alkyl, N(C₁-C₄ alkyl)(C₁-C₄ alkyl) C₁-C₄ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₄ alkoxy C₁-C₄ alkyl, or OH, each of which is

optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃; and

R₁₈ is C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₄ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH.

Embodiment A87. Compounds according to embodiment A80, wherein

R₅ is benzyl or phenethyl, wherein each is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, halogen, C₁-C₆ alkoxy, CO₂H, -(C₁-C₄ alkyl)-CO₂H, C₁-C₆ thioalkoxy, amidinooxime, C₁-C₆ alkoxycarbonyl, -(C₁-C₄ alkyl)-C₁-C₆ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, -(C₁-C₄ alkyl)-CN, CN, phenyl C₁-C₆ alkoxy, OH, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈, amidinooxime, -SO₂(C₁-C₆ alkyl), -O-CH₂-O-, -O-CH₂CH₂-O-, phenyl C₁-C₄ alkoxy, or phenyl; wherein R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl, thiomorpholinyl, ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen,

R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A88. Compounds according to embodiment A87, wherein

5 R₅ is benzyl which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄alkyl)-C(O)NR₆R₇, halogen, C₁-C₄ alkoxy, CO₂H, C₁-C₄ thioalkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, CN, OH, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -SO₂(C₁-C₆ alkyl), or
10 benzyloxy; and wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, or -SO₂(C₁-C₆ alkyl), each of
15 which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

In this embodiment, it is preferred that R₆ and R₇ are not
20 simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A89. Compounds according to embodiment A80, wherein

25 R₅ is benzyl which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, -(C₁-C₄alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, NR₈R₉, halogen, C₁-C₄ alkoxy, C₁-C₄ thioalkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ hydroxyalkyl, or CN; wherein

30 R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or C₁-C₄ alkoxy C₁-C₄ alkyl, each of which is

optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH.

Embodiment A90. Compounds according to embodiment A89, wherein

the R₅ group is disubstituted with two groups that are meta to each other.

Embodiment A91. Compounds according to embodiment A78, wherein

R₅ is phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, -NR₆R₇, NR₆R₇(C₁-C₆ alkyl), NR₈R₉, C₁-C₆ hydroxyalkyl, halogen, C₁-C₄ alkoxy, CO₂H, OH, C₁-C₆ alkoxycarbonyl, carboxaldehyde, C₁-C₄ haloalkyl, -(C₁-C₄ alkyl)-NR₁₅C(O)NR₁₆R₁₇, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈; wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or C₁-C₆ alkanoyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen,

R₁₅ is H or C₁-C₆ alkyl;

R₁₆ and R₁₇ are independently H or C₁-C₆ alkyl; or

R₁₆, R₁₇, and the nitrogen to which they are attached form a morpholinyl ring;

5 R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

10 In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH.

Embodiment A92. Compounds according to embodiment A91, wherein

15 R₅ is phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -(C₁-C₄ alkyl)-C(O)NR₆R₇, -C(O)NR₆R₇, -NR₆R₇, NR₆R₇(C₁-C₆ alkyl), NR₈R₉, C₁-C₆ hydroxyalkyl, halogen, C₁-C₄ alkoxy, CO₂H, OH, C₁-C₆ alkoxy carbonyl, carboxaldehyde, C₁-C₄ haloalkyl, -(C₁-C₄ alkyl)-NR₁₅C(O)NR₁₆R₁₇, -(C₁-C₄ alkyl)-NR₁₅C(O)R₁₈;
20 wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl), -SO₂NH₂,
25 -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or C₁-C₆ alkanoyl each of which is optionally substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃;

30 R₁₅ is H or C₁-C₆ alkyl;

R₁₆ and R₁₇ are independently H or C₁-C₆ alkyl; or

R₁₆, R₁₇, and the nitrogen to which they are attached form a morpholinyl ring;

R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

5

Embodiment A93. Compounds according to embodiment A92, wherein

R₁ is halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, or carboxaldehyde;

10 R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, 15 pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, or hydroxy(C₁-C₄)alkyl.

20

Embodiment A94. Compounds according to embodiment A93, wherein

R₅ is phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, -C(O)NR₆R₇, 25 -(C₁-C₄ alkyl)-C(O)NR₆R₇, -NR₆R₇, NR₆R₇(C₁-C₆ alkyl), C₁-C₆ hydroxyalkyl, halogen, C₁-C₄ alkoxy, CO₂H, OH, C₁-C₆ alkoxycarbonyl, carboxaldehyde, C₁-C₄ haloalkyl, wherein

R₆ and R₇ at each occurrence are independently H, OH, C₁-C₆ alkyl, amino C₁-C₄ alkyl, NH(C₁-C₆ alkyl)alkyl, N(C₁-C₆ alkyl)(C₁-C₆ alkyl) C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, 30 C₁-C₆ alkoxy C₁-C₆ alkyl, -SO₂(C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or C₁-C₆ alkanoyl, each of which is optionally

substituted with 1, 2, or 3 groups that are independently halogen, OH, SH, C₃-C₆ cycloalkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl, OH, CF₃, or OCF₃;

5

Embodiment A101. Compounds according to embodiment A66, wherein

R₅ is thienyl(C₁-C₆ alkyl), piperidinyl(C₁-C₆)alkyl,
 10 pyrrolidinyl(C₁-C₆)alkyl, imidazolidinyl(C₁-C₆)alkyl,
 piperazinyl(C₁-C₆)alkyl, pyridyl(C₁-C₆)alkyl, pyrimidyl(C₁-
 C₆)alkyl, pyridazyl(C₁-C₆)alkyl, pyrazinyl(C₁-C₆)alkyl,
 isoquinolinyl(C₁-C₆)alkyl, tetrahydroisoquinolinyl(C₁-
 C₆)alkyl, indolyl(C₁-C₆)alkyl, 1H-indazolyl(C₁-C₆)alkyl,
 15 dihydroindolonyl(C₁-C₆ alkyl), indolinyl(C₁-C₆ alkyl),
 dihydroisoindolyl(C₁-C₆ alkyl), dihydrobenzimidazolyl(C₁-C₆
 alkyl), or dihydrobenzoimidazolonyl(C₁-C₆ alkyl), wherein
 each of the above is unsubstituted or substituted with 1,
 2, 3, 4, or 5 groups that are independently (C₁-
 20 C₆)alkyl, halogen, (C₁-C₆)alkoxy, (C₁-C₆)hydroxyalkyl,
 phenyl(C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, (C₁-
 C₆)alkoxycarbonyl, phenyl(C₁-C₆)alkoxycarbonyl, OH,
 CO₂H, CN, amidinooxime, NR₈R₉, NR₆R₇-(C₁-C₆ alkyl)-, -
 C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, amidino,
 25 piperazinyl, morpholinyl, -SO₂ (C₁-C₆) alkyl, -SO₂NH₂,
 -SO₂NH(C₁-C₆)alkyl, -SO₂N(C₁-C₆)alkyl (C₁-C₆)alkyl,
 (C₁-C₄)haloalkyl, -(C₁-C₄ alkyl)-NR₁₅C(O)NR₁₆R₁₇, -(C₁-
 C₄ alkyl)-NR₁₅C(O)R₁₈, -O-CH₂-O-, -O-CH₂CH₂-O-, or (C₁-
 C₄)haloalkoxy; wherein
 30 R₆ and R₇ are independently at each occurrence H,
 (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-
 C₆)alkyl, (C₁-C₆)alkoxycarbonyl, (C₁-
 C₆)hydroxyalkyl, -(C₁-C₄)alkyl-CO₂-(C₁-C₆)alkyl,

(C₁-C₆)alkanoyl, phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy, or phenyl(C₁-C₆)alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, (C₁-C₄)alkoxy, OH, SH, C₃-C₆ cycloalkyl, NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), (C₁-C₄)alkyl, CF₃ or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen; and

R₁₈ is C₁-C₆ alkyl optionally substituted with -O-(C₂-C₆ alkanoyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl; amino C₁-C₆ alkyl, mono or dialkylamino C₁-C₆ alkyl.

In this embodiment, it is preferred that R₆ and R₇ are not simultaneously OH; and

R₆ and R₇ are not simultaneously -SO₂(C₁-C₆ alkyl).

Embodiment A102. Compounds according to embodiment A101, wherein

R₁ is halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, or carboxaldehyde;

R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, (C₁-C₄) alkyl optionally substituted with one or two groups that are independently CO₂H, -CO₂alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, or hydroxy(C₁-C₄)alkyl.

5

Embodiment A103. Compounds according to embodiment A102, wherein

R₅ is thienyl(C₁-C₆ alkyl), indolyl(C₁-C₆ alkyl), pyridinyl(C₁-C₆ alkyl), piperazinyl(C₁-C₆ alkyl), or pyrazinyl(C₁-C₆ alkyl) each of which is optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, C₁-C₆ alkoxycarbonyl, -NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, haloalkyl, C₁-C₆ alkanoyl,

10

15

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxycarbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

20

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

25

Embodiment A104. Compounds according to embodiment A103, wherein

R₅ is thienyl(C₁-C₆ alkyl), indolyl(C₁-C₆ alkyl), pyridinyl(C₁-C₆ alkyl), piperazinyl(C₁-C₆ alkyl), or pyrazinyl(C₁-C₆ alkyl).

30

Embodiment A105. Compounds according to embodiment A103, wherein

R₄ is H, methyl, ethyl, or -CH₂OH;

R₅ is pyridinyl(C₁-C₆ alkyl), or pyrazinyl(C₁-C₆ alkyl) each of which is optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, C₁-C₆ alkoxy carbonyl, -NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, CF₃, C₁-C₆ alkanoyl, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A106. Compounds according to embodiment A105, wherein

R₄ is H, alkyl substituted with one or two groups that are independently CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇.

Embodiment A112. Compounds according to embodiment 16, wherein

R₁ is halogen, or methyl;

R₂ is benzyloxy, which is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, CF₃, OCF₃, or (C₁-C₄) alkyl,; and

R₄ is H, methyl, ethyl, -CH₂OH, -CH₂CO₂-(C₁-C₄ alkyl), or C₂ hydroxyalkyl.

Embodiment A113. Compounds according to any one of
embodiments A85, A95, A97, A98, A99, A100, 16 or 17, wherein
R₁ is halogen, or methyl;

5 R₂ is benzyloxy, which is optionally substituted with 1, 2, 3,
or 4 groups that are independently halogen, -(C₁-C₆)alkyl-
N(R)-CO₂R₃₀, CF₃, OCF₃, or (C₁-C₄) alkyl,; and
R₄ is alkyl substituted with one group that is CO₂H, -CO₂-(C₁-
C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-
10 C₆)alkoxy, or -NR₆R₇.

Embodiment A114. Compounds according to embodiment
A66, wherein

R₅ is isoquinolinyl(C₁-C₆ alkyl), tetrahydroisoquinolinyl(C₁-C₆
15 alkyl), 1H-indazolyl(C₁-C₆ alkyl), dihydroindolonyl(C₁-C₆
alkyl), indolinyl(C₁-C₆ alkyl), dihydroisoindolyl(C₁-C₆
alkyl), dihydrobenzimidazolyl(C₁-C₆ alkyl),
dihydrobenzoimidazolonyl(C₁-C₆ alkyl), each of which is
unsubstituted or substituted with 1, 2, or 3 groups that
20 are independently alkyl, alkoxy, halogen, C₁-C₆
alkoxycarbonyl, alkanoyl optionally substituted with 1 or
2 groups that are independently selected from the group
consisting of OH, NH₂, NH(C₁-C₆ alkyl), and N(C₁-C₆ alkyl)
(C₁-C₆ alkyl), -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-
25 (C₁-C₆ alkyl)-, -NR₆R₇, or SO₂H; or
piperidinyl C₁-C₄ alkyl optionally substituted with 1, 2, or 3
groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy,
halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆
alkyl)-, or -NR₆R₇, or C₁-C₆ alkoxycarbonyl.

30

Embodiment A115. Compounds according to embodiment
A114, wherein

R₅ is isoquinolinyl(C₁-C₄ alkyl), piperidinyl C₁-C₄ alkyl, tetrahydroisoquinolinyl(C₁-C₄ alkyl), 1H-indazolyl(C₁-C₄ alkyl), dihydroindolonyl(C₁-C₄ alkyl), indolinyl(C₁-C₄ alkyl), dihydroisoindolyl(C₁-C₄ alkyl), dihydrobenzimidazolyl(C₁-C₄ alkyl), or dihydrobenzoimidazolonyl(C₁-C₄ alkyl).

Embodiment A116. Compounds according to embodiment A114, wherein

R₅ is piperidinyl C₁-C₄ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, halogen, or C₁-C₆ alkoxycarbonyl.

Embodiment A117. Compounds according to embodiment A66, wherein

R₅ is pyrimidyl, indolinyl, indolyl, 1H-isoindolyl, isoquinolinyl, tetrahydroisoquinolinyl, benzimidazolyl, dihydro-1H-benzimidazolyl, pyrrolyl, imidazolyl, or each of which is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of C₁-C₆ alkoxycarbonyl, C₁-C₄ thioalkoxy, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, alkyl, alkoxy, halogen, C₁-C₆ alkoxycarbonyl, or alkanoyl optionally substituted with 1 or 2 groups that are independently selected from the group consisting of OH, NH₂, NH(C₁-C₆ alkyl), and N(C₁-C₆ alkyl) (C₁-C₆ alkyl), and SO₂H; or pyridyl, pyrazolyl, optionally substituted with 1, 2, or 3 groups that are independently -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, C₁-C₄ alkyl, C₁-C₄ hydroxyalkyl, halogen, C₁-C₆

alkoxycarbonyl, $-NR_6R_7$, $NR_6R_7-(C_1-C_6 \text{ alkyl})-$, CF_3 , C_1-C_6 alkanoyl, wherein

R_6 and R_7 at each occurrence are independently H, C_1-C_6 alkyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxycarbonyl, halogen, C_3-C_6 cycloalkyl, OH, SH, or C_1-C_4 alkoxy;

or

R_6 , R_7 , and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C_1-C_4 alkyl, or halogen.

Embodiment A118. Compounds according to embodiment A117, wherein

R_5 is pyrimidyl, pyrrolyl, imidazolyl, or pyrazolyl, each of which is optionally substituted with 1, 2, or 3 groups independently selected from C_1-C_6 alkoxycarbonyl, C_1-C_4 thioalkoxy, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently alkyl, alkoxy, halogen, C_1-C_6 alkoxycarbonyl, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$, $NR_6R_7-(C_1-C_6 \text{ alkyl})-$, or $-NR_6R_7$, or C_1-C_4 alkanoyl optionally substituted with 1 or 2 groups that are independently selected from the group consisting of OH, NH_2 , $NH(C_1-C_6 \text{ alkyl})$, and $N(C_1-C_6 \text{ alkyl}) (C_1-C_6 \text{ alkyl})$, or SO_2H .

Embodiment A119. Compounds according to embodiment A117, wherein

R_5 is pyridyl or pyrazolyl, optionally substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkyl, C_1-C_4 hydroxyalkyl, halogen, $-C(O)NR_6R_7$, $-(C_1-C_4 \text{ alkyl})-C(O)NR_6R_7$,

NR₆R₇-(C₁-C₆ alkyl)-, or -NR₆R₇, C₁-C₆ alkoxy carbonyl, -
NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, CF₃, C₁-C₆ alkanoyl, wherein
R₆ and R₇ at each occurrence are independently H, C₁-C₆
alkyl optionally substituted with 1, 2, or 3 groups
5 that are independently C₁-C₄ alkoxy carbonyl, halogen,
C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;
or

R₆, R₇, and the nitrogen to which they are attached form a
piperidiny, pyrrolidiny, piperaziny, or a
10 morpholiny ring optionally substituted with 1 or 2
groups that are independently alkyl, hydroxy,
hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A120. Compounds according to embodiment
15 A119, wherein

R₅ is pyridyl or pyrazolyl, optionally substituted with 1, 2,
or 3 groups that are independently C₁-C₄ alkyl, C₁-C₄
hydroxyalkyl, halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇,
NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, C₁-C₆ alkoxy carbonyl, CF₃, C₁-
20 C₆ alkanoyl, wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl
optionally substituted with 1, 2, or 3 groups that are
independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆
cycloalkyl, OH, SH, or C₁-C₄ alkoxy.

25 Embodiment A121. Compounds according to embodiment
A119, wherein

R₅ is pyridyl or pyrazolyl, optionally substituted with 1, 2,
or 3 groups that are independently C₁-C₄ alkyl, C₁-C₄
30 hydroxyalkyl, halogen, -C(O)NR₆R₇, -(C₁-C₄ alkyl)-C(O)NR₆R₇,
NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, C₁-C₆ alkoxy carbonyl, CF₃, C₁-
C₆ alkanoyl, wherein

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A122. Compounds according to any one of embodiments A114, A115, A116, or A117 wherein

R₁ is halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, or carboxaldehyde;

R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, (C₁-C₄) alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, hydroxy(C₁-C₄)alkyl.

Embodiment A123. Compounds according to embodiment A66, wherein

R₅ is C₁-C₆ alkyl optionally substituted with 1 or 2, groups that are independently C₁-C₄ alkoxy carbonyl, or halogen, or

R₅ is C₁-C₄ alkoxy, ethyl, methyl, cyclopropylmethyl, cycloalkyl, or alkynyl, or

R₅ is C₂-C₆ alkenyl optionally substituted with C₁-C₄ alkoxy carbonyl or cyclohexyl.

Embodiment A124. Compounds according to embodiment A123, wherein

R₁ is halogen, methyl, ethyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, or carboxaldehyde;

R₂ is benzyloxy, OH, phenyloxy, phenyloxy(C₁-C₆)alkyl, or phenyl (C₁-C₄) thioalkoxy, wherein each of the above is optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, NR₆R₇, (C₁-C₄) haloalkyl, (C₁-C₄) haloalkoxy, (C₁-C₆) alkyl, pyridyl, or NR₆R₇-(C₁-C₆ alkyl)-; and

R₄ is H, (C₁-C₄) alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, hydroxy(C₁-C₄)alkyl; wherein

R₆ and R₇ at each occurrence are independently H, C₁-C₆ alkyl optionally substituted with 1, 2, or 3 groups that are independently C₁-C₄ alkoxy carbonyl, halogen, C₃-C₆ cycloalkyl, OH, SH, or C₁-C₄ alkoxy;

or

R₆, R₇, and the nitrogen to which they are attached form a piperidinyl, pyrrolidinyl, piperazinyl, or a morpholinyl ring optionally substituted with 1 or 2 groups that are independently alkyl, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A125. Compounds according to embodiment A124, wherein

R₅ is C₁-C₆ alkyl optionally substituted with 1 or 2, groups that are independently C₁-C₄ alkoxy carbonyl, or halogen, or

R₅ is C₁-C₄ alkoxy, ethyl, methyl, cyclopropylmethyl, cyclohexyl, cyclopentyl, C₂-C₆ alkynyl, or

R₅ is C₂-C₆ alkenyl optionally substituted with C₁-C₄ alkoxy carbonyl or cyclohexyl.

Embodiment A126. Compounds according to embodiment A66, wherein

R_2 is phenylalkynyl, $-OC(O)NH(CH_2)_n\text{aryl}$, $-OC(O)N(\text{alkyl})(CH_2)_n\text{aryl}$, $-OSO_2(C_1-C_6)\text{alkyl}$, $-OSO_2\text{aryl}$, or NR_8R_9 , wherein

n is 0, 1, 2, 3, 4, 5 or 6;

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, $-(C_1-C_6)\text{alkyl}-N(R)-CO_2R_{30}$, alkoxy, alkoxycarbonyl, CN, NR_6R_7 , haloalkyl, haloalkoxy, alkyl, heteroaryl, heteroarylalkyl, $NR_6R_7-(C_1-C_6\text{ alkyl})-$, phenyl, $-SO_2$ -phenyl wherein the phenyl groups are optionally substituted with 1, 2, or 3 groups that are independently halogen or NO_2 ; or $-OC(O)NR_6R_7$, wherein

R_6 and R_7 are independently at each occurrence H, alkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, $-SO_2$ -alkyl, OH, hydroxyalkyl, $-(C_1-C_4)\text{alkyl}-CO_2$ -alkyl, heteroarylalkyl, alkanoyl, arylalkyl, arylalkoxy, or arylalkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, heterocycloalkyl, OH, NH_2 , C_3-C_6 cycloalkyl, $NH(\text{alkyl})$, $N(\text{alkyl})(\text{alkyl})$, $-O$ -alkanoyl, alkyl, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy; or

R_6 , R_7 , and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, hydroxy, hydroxy C_1-C_4 alkyl, or halogen.

Embodiment A127. Compounds according to embodiment A126, wherein

R_1 is halogen, methyl, ethyl, C_2 - C_4 alkenyl, C_2 - C_4 alkynyl, or carboxaldehyde; and

5 R_4 is H, $(C_1$ - $C_4)$ alkyl substituted with one group that is CO_2H , $-CO_2-(C_1-C_6)$ alkyl, $-C(O)NRR$, $-N(R_{30})C(O)NRR$, $-N(R_{30})C(O)-(C_1-C_6)$ alkoxy, $-NR_6R_7$, $NR_6R_7-(C_1-C_6)$ alkyl-, or hydroxy (C_1-C_4) alkyl.

10 Embodiment A128. Compounds according to embodiment A127, wherein

R_5 is phenyl, optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, CF_3 , OCF_3 , $-(C_1-C_4)$ alkyl- $C(O)NR_6R_7$, $NR_6R_7-(C_1-C_6)$ alkyl-,
15 $-NR_6R_7$, or $C(O)NR_6R_7$, wherein

R_6 and R_7 are independently at each occurrence H, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 alkoxy C_1 - C_6 alkyl, C_1 - C_6 alkoxy carbonyl, OH, C_1 - C_6 hydroxyalkyl, $-(C_1-C_4)$ alkyl- CO_2 -alkyl, pyridyl C_1 - C_6 alkyl, C_1 - C_6 alkanoyl, benzyl, phenyl C_1 - C_6 alkoxy, or phenyl C_1 - C_6 alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C_1 - C_6 alkoxy, piperidinyl C_1 - C_6 alkyl, morpholinyl C_1 - C_6 alkyl,
20 piperazinyl C_1 - C_6 alkyl, OH, SH, C_3 - C_6 cycloalkyl, NH_2 , $NH(alkyl)$, $N(alkyl)(alkyl)$, $-O-C_1-C_4$ alkanoyl, C_1 - C_4 alkyl, CF_3 , or OCF_3 ; or

R_6 , R_7 , and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl,
30 pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy, hydroxy C_1 - C_4 alkyl, or halogen; or

R₅ is benzyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, CN, CF₃, OCF₃, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, or C(O)NR₆R₇.

5

Embodiment A129. Compounds according to embodiment A128, wherein

R₂ is NR₈R₉, or NR₈R₉-(C₁-C₄ alkyl)-; wherein

10 R₈ at each occurrence is independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl(C₁-C₆)alkyl or phenyl(C₁-C₆)alkanoyl wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxycarbonyl, halogen, or C₁-C₄ haloalkyl; and

15 R₉ at each occurrence is independently C₁-C₆ alkyl, C₁-C₆ alkanoyl, phenyl(C₁-C₆)alkyl, C₃-C₇ cycloalkyl, C₂-C₆ alkenyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, C₃-C₇ cycloalkyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkanoyl, -SO₂-phenyl, and phenyl
20 wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxycarbonyl, halogen, or C₁-C₄ haloalkyl.

25 Embodiment A130. Compounds according to embodiment A129, wherein

R₈ is H.

30 Embodiment A131. Compounds according to embodiment A130, wherein

R₂ is -NH-benzyl optionally substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, CF₃, OCF₃,

or

R₂ is -NH-C(O)phenyl, wherein the phenyl group is optionally substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkyl, or C₁-C₄ alkoxy; or

5 R₂ is -NH-allyl.

Embodiment A132. Compounds according to embodiment A131, wherein

R₁ is chloro, bromo, iodo, or methyl; and

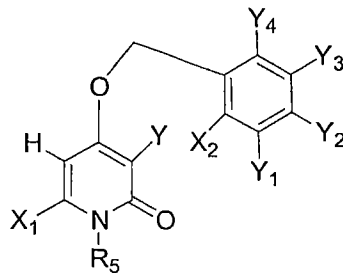
10 R₅ is benzyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, C₁-C₆ alkyl, C₁-C₆ alkoxy, CN, CF₃, OCF₃, or C(O)NR₆R₇.

15 Embodiment A133. Compounds according to embodiment A131, wherein

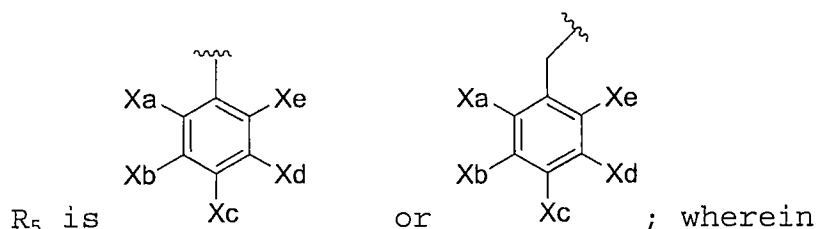
R₁ is chloro, bromo, iodo, or methyl; and

R₅ is phenyl, optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₄ alkyl)-C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -NR₆R₇, C₁-C₄ alkyl, C₁-C₄ alkoxy, CF₃, OCF₃, or C(O)NR₆R₇.

Embodiment A134. A compound of the formula



25 or pharmaceutically acceptable salts thereof, wherein



X₁, X₂, X_a, X_b, X_c, X_d, and X_e are independently selected from
 -C(O)NR₆R₇, -NR₆R₇, hydroxy(C₁-C₄)alkyl, H, OH, halogen,
 haloalkyl, alkyl, haloalkoxy, heteroaryl,
 5 heterocycloalkyl, C₃-C₇ cycloalkyl, NR₆R₇-(C₁-C₆ alkyl)-, -
 CO₂-(C₁-C₆)alkyl, -N(R)C(O)NR₆R₇, -N(R)C(O)-(C₁-C₆)alkoxy,
 CO₂H-(C₁-C₆ alkyl)-, or -SO₂NR₆R₇; wherein

the heteroaryl and heterocycloalkyl groups are optionally
 substituted with -NR₆R₇, -C(O)NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-,
 10 C₁-C₆ alkyl, C₁-C₆ alkoxy, or halogen;

R₆ and R₇ are independently at each occurrence H, C₁-C₆
 alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆
 alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, C₁-C₆
 thiohydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-
 15 C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy,
 or phenyl C₁-C₆ alkanoyl, wherein each of the above
 is unsubstituted or substituted with 1, 2, or 3
 groups that are independently, halogen, C₃-C₆
 cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl,
 20 morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH,
 SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄
 alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a
 morpholinyl, thiomorpholinyl, piperidinyl,
 25 pyrrolidinyl, or piperazinyl ring which is
 optionally substituted with 1 or 2 groups that are
 independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy,
 hydroxy C₁-C₄ alkyl, or halogen;

R at each occurrence is independently H or C₁-C₆ alkyl;
and

Y, Y₁, Y₂, Y₃, and Y₄ are independently selected from H,
halogen, alkyl, carboxaldehyde, hydroxyalkyl, alkenyl,
5 alkynyl, CN, alkanoyl, alkoxy, alkoxyalkyl, haloalkyl,
and carboxyl.

Embodiment A135. Compounds according to embodiment
A134, wherein

10 Y₂, Y₄, and Y are independently halogen; and
Y₁ and Y₃ are both hydrogen.

Embodiment A136. Compounds according to embodiment
A135, wherein

15 X₁ is H, methyl, -NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, C₁-C₆
hydroxyalkyl, or -(C₁-C₄ alkyl)-morpholinyl.

Embodiment A137. Compounds according to embodiment
A136, wherein

20 X_a and X_e are independently halogen, is NH₂, NH(C₁-C₆ alkyl),
N(C₁-C₆ alkyl)(C₁-C₆ alkyl) or methyl.

Embodiment A138. Compounds according to embodiment
A137, wherein

25 X_b or X_c is -NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, -SO₂NR₆R₇, or
halogen; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆
alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆
alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, -(C₁-C₄)alkyl-
30 CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl,
benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl,
wherein each of the above is unsubstituted or
substituted with 1, 2, or 3 groups that are

independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A139. Compounds according to embodiment A138, wherein

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A140. Compounds according to embodiment A138, wherein

R₆, R₇, and the nitrogen to which they are attached form a piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A141. Compounds according to embodiment A138, wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl

C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃.

Embodiment A142. Compounds according to embodiment A138, wherein R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, or C₁-C₆ alkanoyl, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently OH, SH, halogen, or C₃-C₆ cycloalkyl.

Embodiment A143. Compounds according to embodiment A137, wherein X_a and X_e are independently fluoro, chloro, or methyl; and X_c is hydrogen or halogen.

Embodiment A144. Compounds according to embodiment A137, wherein X_a is halogen; X_e is NH₂, NH(C₁-C₆ alkyl) or N(C₁-C₆ alkyl)(C₁-C₆ alkyl); X_b and X_d are both hydrogen.

Embodiment A145. Compounds according to embodiment A144, wherein X_c is -NR₆R₇, NR₆R₇ C₁-C₆ alkyl, -SO₂NR₆R₇, or halogen; wherein R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, -(C₁-C₄)alkyl-

CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A146. Compounds according to embodiment A145, wherein

X_c is fluoro, chloro, NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), -SO₂NH₂, -SO₂NH(C₁-C₆ alkyl), -SO₂N(C₁-C₆ alkyl)(C₁-C₆ alkyl), or piperazinyl, wherein the piperazinyl group is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A147. Compounds according to either embodiment A137 or A144, wherein

X_c is -C(O)NR₆R₇, -(C₁-C₆ alkyl)-C(O)NR₆R₇, NR₆R₇, or NR₆R₇-(C₁-C₆ alkyl)-; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl,

benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A148. Compounds according to embodiment A147, wherein

R₆ is hydrogen; and

R₇ is C₁-C₆ alkyl or C₁-C₆ alkanoyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), OH, SH, cyclopropyl, or C₁-C₄ alkoxy.

Embodiment A148a. Compounds according to embodiment A148, wherein

R₇ is C₁-C₆ alkanoyl optionally substituted with 1, 2, or 3 groups that are independently OH, cyclopropyl, or NH₂.

Embodiment A149. Compounds according to embodiment A135, wherein

X_a is hydrogen;

X_b, X_c, or X_d is -C(O)NR₆R₇, -(C₁-C₆ alkyl)-C(O)NR₆R₇, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)- or -CO₂-(C₁-C₆)alkyl; wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, -(C₁-C₄)alkyl-CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl, benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen; and

X_e is hydrogen, methyl, C₁-C₂ alkoxy, or halogen.

Embodiment A150. Compounds according to embodiment A149, wherein

X_b is NR₆R₇, or NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇ or -CO₂-(C₁-C₆)alkyl; wherein

R₆ is hydrogen or C₁-C₄ alkyl;

R₇ is OH, C₁-C₆ alkyl or C₁-C₆ alkanoyl, wherein the alkyl and alkanoyl groups substituted with 1, 2, or 3 groups that are independently NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₆ alkyl), C₃-C₆ cycloalkyl, OH, or C₁-C₄ alkoxy.

Embodiment A151. Compounds according to embodiment A137, wherein

X_a is halogen;

X_b is NR_6R_7 , $NR_6R_7-(C_1-C_6 \text{ alkyl})-$, $-C(O)NR_6R_7$, or $-CO_2-(C_1-C_6)alkyl$;

X_c is NR_6R_7 , $NR_6R_7-(C_1-C_6 \text{ alkyl})-$, $-C(O)NR_6R_7$, halogen, $-CO_2-(C_1-C_6)alkyl$, NH_2 , $NH(C_1-C_6 \text{ alkyl})$, $N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$,
 5 $-SO_2NH_2$, $-SO_2NH(C_1-C_6 \text{ alkyl})$, $-SO_2N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, or piperazinyl, wherein the piperazinyl group is optionally substituted with 1 or 2 groups that are independently $C_1-C_4 \text{ alkyl}$, $C_1-C_4 \text{ alkoxy}$, hydroxy, hydroxy $C_1-C_4 \text{ alkyl}$, or halogen;

10 X_d is hydrogen;

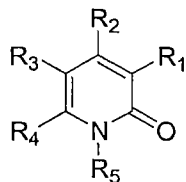
X_e is H, methyl, NH_2 , $NH(C_1-C_6 \text{ alkyl})$ or $N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$.

Embodiment A152. Compounds according to embodiment
 15 A135, wherein

X_1 , X_2 , X_a , X_b , X_c , X_d , and X_e are independently selected from H, OH, halogen, CF_3 , alkyl, OCF_3 , pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, thienyl, furyl, pyrrolyl, piperidinyl, piperazinyl, or C_3-C_7 cycloalkyl, wherein
 20 each of the above is optionally substituted with $-NR_6R_7$, $-C(O)NR_6R_7$, $NR_6R_7-(C_1-C_6 \text{ alkyl})-$, $C_1-C_6 \text{ alkyl}$, $C_1-C_6 \text{ alkoxy}$, or halogen.

Embodiment A153. Compounds according to embodiment
 25 A152, wherein at least three of X_1 , X_2 , X_a , X_b , X_c , X_d , and X_e are hydrogen.

Embodiment A154. A compound of the formula:



30 or a pharmaceutically acceptable salt thereof, wherein

R₁ is alkanoyl, halogen, arylalkanoyl, arylalkyl, alkoxyalkyl, hydroxyalkyl, or carboxaldehyde, wherein

the aryl portion of arylalkyl, and arylalkanoyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, haloalkyl, haloalkoxy or CO₂H;

the alkyl portion of the hydroxyalkyl, arylalkyl, alkanoyl, alkoxyalkyl and arylalkanoyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, ethoxy or spirocyclopropyl;

R₂ is arylalkoxy, aryloxy, phenyloxy(C₁-C₆)alkyl, OH, halogen, arylthioalkoxy, alkoxy, -OC(O)NH(CH₂)_naryl, -OC(O)N(alkyl)(CH₂)_naryl, alkyl, alkoxyalkoxy, dialkylamino, pyridyl, pyrimidyl, pyridazyl, pyrazolyl, imidazolyl, pyrrolyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, tetrazolyl, pyrazinyl, benzimidazolyl, triazinyl, tetrahydrofuryl, piperidinyl, hexahydropyrimidinyl, thiazolyl, thienyl, or CO₂H, wherein n is 0, 1, 2, 3, 4, 5 or 6;

the aryl portion of arylalkoxy, aryloxy, arylthioalkoxy, -OC(O)NH(CH₂)_naryl, and -OC(O)N(alkyl)(CH₂)_naryl or the heteroaryl and heterocycloalkyl groups is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, haloalkyl, heteroaryl, heteroarylalkyl, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -OC(O)NR₆R₇, wherein

R₆ and R₇ are independently at each occurrence H, alkyl, alkoxy, alkanoyl, arylalkyl, arylalkoxy, or arylalkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, SH,

C₃-C₆ cycloalkyl, alkoxy, alkyl, haloalkyl, or haloalkoxy; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, or halogen;

R at each occurrence is independently H or C₁-C₆ alkyl;

R₃₀ is C₁-C₆ alkyl optionally substituted with 1 or 2 groups that are independently OH, SH, halogen, amino, monoalkylamino, dialkylamino or C₃-C₆ cycloalkyl;

R₃ is halogen, arylalkoxy carbonyl, aryloxy carbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl, arylalkoxy, -OC(O)N(alkyl)(CH₂)_naryl, aryloxy, arylthio, thioalkoxy, arylthioalkoxy, alkenyl, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, or alkyl, wherein the aryl portion of arylalkoxy carbonyl, aryloxy carbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl, arylalkoxy, -OC(O)N(alkyl)(CH₂)_naryl, and arylthioalkoxy, is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, alkyl, haloalkyl, or haloalkoxy, wherein n is 0, 1, 2, 3, 4, 5, or 6; or

R₄ is H, alkyl substituted with one group selected from CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, and -NR₆R₇, arylalkoxy, arylalkyl, hydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein

the aryl portion of arylalkoxy, arylalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy; and

5 R₅ is arylalkyl, alkyl, aryl, alkoxy, heterocycloalkylalkyl, heteroarylalkyl, arylthioalkyl, heterocycloalkyl, or heteroaryl, wherein

each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, arylalkoxy, thioalkoxy, 10 alkoxycarbonyl, arylalkoxycarbonyl, CO₂H, CN, amidinoxime, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, haloalkyl, or haloalkoxy.

15

Embodiment A160. Compounds according to embodiment A154 wherein

R₁ is halogen, (C₁-C₆)alkanoyl, phenyl(C₁-C₆)alkanoyl, 20 naphthyl(C₁-C₆)alkanoyl, naphthyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkyl, alkoxyalkyl, hydroxyalkyl, or carboxaldehyde, wherein

the phenyl and naphthyl portions of the above are unsubstituted or substituted with 1, 2, 3, 4, or 5 25 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, CF₃, OCF₃ or CO₂H;

the alkyl portion of the above groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy.

30 R₂ is phenylalkoxy, aryloxy, phenyloxy(C₁-C₆)alkyl, OH, halogen, phenylthioalkoxy, alkoxy, alkyl, alkoxyalkoxy, -OC(O)NH(CH₂)_nphenyl, -OC(O)N(alkyl)(CH₂)_nphenyl, pyridyl, pyrimidyl, pyridazyl, pyrazolyl, or thienyl, wherein

n is 0, 1, 2, 3, or 4, and

the above groups are unsubstituted or substituted with 1,
2, 3, 4, or 5 groups that are independently halogen,
-(C₁-C₆)alkyl-N(R)-CO₂R₃₀, halo(C₁-C₄)alkyl, or
thienyl;

R₃ is halogen, phenylalkoxycarbonyl, phenyloxycarbonyl,
phenyl(C₁-C₆)alkyl, phenylalkoxy, phenyloxy, phenylthio,
thioalkoxy, arylthioalkoxy, (C₂-C₆)alkenyl, NR₆R₇, NR₆R₇-
(C₁-C₆ alkyl)-, or alkyl, wherein

the phenyl, naphthyl, and aryl portions of
arylalkoxycarbonyl, aryloxycarbonyl, arylalkyl,
-OC(O)NH(CH₂)_naryl, arylthioalkoxy, arylalkoxy,
and-OC(O)N(alkyl)(CH₂)_naryl, are unsubstituted or
substituted with 1, 2, or 3 groups that are
independently, halogen, alkoxy, alkyl, CF₃, or OCF₃,

wherein n is 0, 1, 2, 3, 4, 5, or 6; or

R₄ is H, (C₁-C₆) alkyl substituted with one group that is CO₂H,
-CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-
(C₁-C₆)alkoxy, or -NR₆R₇, phenylalkoxy, phenyl(C₁-C₆)alkyl,
hydroxyalkyl, haloalkyl, alkoxyalkyl, or alkoxyalkoxy,
wherein

the phenyl portion of the above groups are unsubstituted
or substituted with 1, 2, 3, 4, or 5 groups that are
independently halogen, hydroxy, alkoxy, alkyl,
nitro, CF₃, or OCF₃.

R₅ is phenyl(C₁-C₆)alkyl, (C₁-C₆)alkyl, phenyl, naphthyl,
pyridyl, (C₁-C₆)alkoxy, piperidinyl(C₁-C₆)alkyl,
pyrrolyl(C₁-C₆)alkyl, imidazolidinyl(C₁-C₆)alkyl,
pyrazolyl(C₁-C₆)alkyl, imidazolyl(C₁-C₆)alkyl,
tetrahydropyridinyl(C₁-C₆)alkyl, thienyl(C₁-C₆)alkyl,
phenylthio(C₁-C₆)alkyl, or pyridyl(C₁-C₆)alkyl, wherein
each of the above is unsubstituted or substituted with 1,
2, or 3 groups that are independently (C₁-C₄)alkyl,

fluoro, chloro, bromo, (C₁-C₄)alkoxy, phenyl(C₁-C₄)alkoxy, thio(C₁-C₄)alkoxy, (C₁-C₄)alkoxycarbonyl, phenyl(C₁-C₄)alkoxycarbonyl, CO₂H, CN, amidinoxime, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, CF₃, -CF₂CF₃, OCF₃ or OCF₂CF₃.

Embodiment A161. Compounds according to embodiment A160 wherein

R₁ is halogen, (C₁-C₄)alkanoyl, phenyl(C₁-C₄)alkanoyl, benzyl, phenethyl, phenpropyl, hydroxyalkyl, or carboxaldehyde, wherein

the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, CF₃, OCF₃ or CO₂H;

the alkyl portion of the above groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy;

R₂ is benzyloxy, phenethyloxy, phenpropyloxy, phenbutyloxy, phenyloxy, phenyloxy(C₁-C₆)alkyl, OH, halogen, phenylthioalkoxy, alkoxy, alkyl, alkoxyalkoxy, wherein n is 0, 1, 2, 3, or 4, and

the above groups are unsubstituted or substituted with 1, 2, or 3, groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, halo(C₁-C₄)alkyl, or thienyl;

R₃ is halogen, phenylalkoxycarbonyl, phenyloxycarbonyl, phenyl(C₁-C₆)alkyl, phenylalkoxy, phenyloxy, phenylthio, thioalkoxy, phenylthioalkoxy, (C₂-C₆)alkenyl, NR₆R₇, NR₆R₇ C₁-C₆ alkyl, or alkyl, wherein

the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, (C₁-C₄)alkyl, CF₃, or OCF₃,

R₄ is H, (C₁-C₆) alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenylalkoxy, benzyl, phenethyl, hydroxyalkyl, haloalkyl, alkoxyalkyl, or alkoxyalkoxy, wherein

the phenyl portion of the above groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, (C₁-C₄)alkoxy, (C₁-C₄)alkyl, nitro, CF₃, or OCF₃.

R₅ is benzyl, phenethyl, phenpropyl, phenbutyl, (C₁-C₆)alkyl, phenyl, or pyridyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently (C₁-C₄)alkyl, fluoro, chloro, bromo, (C₁-C₄)alkoxy, phenyl(C₁-C₄)alkoxy, thio(C₁-C₄)alkoxy, (C₁-C₄)alkoxycarbonyl, CO₂H, CN, amidinooxime, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, CF₃, or OCF₃.

Embodiment A162. Compounds according to embodiment A161 wherein

R₁ is bromo, phenyl(C₁-C₄)alkanoyl, benzyl, phenethyl, phenpropyl, hydroxyalkyl, or carboxaldehyde, wherein the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, CF₃, OCF₃ or CO₂H;

R₂ is benzyloxy, phenethyloxy, phenpropyloxy, phenbutyloxy, phenyloxy, phenyloxy(C₁-C₆)alkyl, OH, halogen, or phenylthioalkoxy, wherein n is 0, 1, 2, 3, or 4, and

the above groups are unsubstituted or substituted with 1, 2, or 3, groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, halo(C₁-C₄)alkyl, or thienyl;

R₃ is bromo, phenylalkoxycarbonyl, phenyloxycarbonyl, phenyl(C₁-C₆)alkyl, phenylalkoxy, phenyloxy, phenylthio, thioalkoxy, phenylthioalkoxy, (C₂-C₆)alkenyl, NR₆R₇, NR₆R₇ C₁-C₆ alkyl, or alkyl, wherein

5 the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, (C₁-C₄)alkyl, CF₃, or OCF₃,

R₄ is H, (C₁-C₆) alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenylalkoxy, benzyl, or phenethyl, wherein

10 the phenyl portion of the above groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, (C₁-C₄)alkoxy, (C₁-C₄)alkyl, nitro, CF₃, or OCF₃.

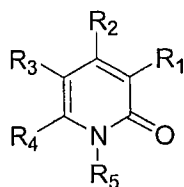
15 R₅ is benzyl, phenethyl, phenpropyl, (C₁-C₆)alkyl, phenyl, or pyridyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently (C₁-C₄)alkyl, fluoro, chloro, bromo, (C₁-C₄)alkoxy, CO₂H, CN, amidinooxime, amidino, CF₃, OCF₃, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, or -C(O)NR₆R₇; wherein

20 R₆ and R₇ are independently hydrogen, OH, C₁-C₄ alkoxy, C₁-C₆ alkanoyl, or C₁-C₆ alkyl, wherein each of the above is optionally substituted with 1 or 2 groups that are independently OH, NH₂, C₃-C₆ cycloalkyl, or halogen; or

25 R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

30

Embodiment A163. Compounds of the formula



or pharmaceutically acceptable salts thereof, wherein

R₁ is H, halogen, alkyl, carboxaldehyde, hydroxyalkyl,
 5 arylalkoxy, arylalkyl, CN, alkanoyl, alkoxy, alkoxyalkyl,
 or arylalkanoyl,

wherein the aryl portion of arylalkoxy, arylalkyl, and
 arylalkanoyl is unsubstituted or substituted with 1,
 2, 3, 4, or 5 groups that are independently halogen,
 10 C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, haloalkyl,
 haloalkoxy or CO₂H;

wherein the alkyl portion of the alkyl, hydroxyalkyl,
 arylalkoxy, arylalkyl, alkanoyl, alkoxy, alkoxyalkyl
 and arylalkanoyl groups is unsubstituted or
 15 substituted with 1, 2, or 3 groups that are
 independently halogen, methoxy, ethoxy or
 spirocyclopropyl;

R₂ is H, arylthio, -OC(O)NH(CH₂)_naryl, arylalkyl,
 -OC(O)N(alkyl)(CH₂)_naryl, or arylthioalkoxy, wherein n is
 20 1, 2, 3, 4, or 5; wherein the aryl groups are optionally
 substituted with 1, 2, 3, 4, or 5 groups that are
 independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, C₁-C₄
 alkoxy, C₁-C₄ alkyl, CF₃, or OCF₃;

R at each occurrence is independently H or C₁-C₆ alkyl;

25 R₃₀ is C₁-C₆ alkyl optionally substituted with 1 or 2
 groups that are independently OH, SH, halogen,
 amino, monoalkylamino, dialkylamino or C₃-C₆
 cycloalkyl;

R₃ is halogen, alkoxycarbonyl, arylalkoxycarbonyl,
 30 aryloxycarbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl,

arylalkoxy, $-\text{OC}(\text{O})\text{N}(\text{alkyl})(\text{CH}_2)_n\text{aryl}$, aryloxy, arylthio, thioalkoxy, arylthioalkoxy, alkenyl, NR_6R_7 , $\text{C}_1\text{-C}_6$ alkyl, NR_6R_7 or alkyl, wherein

the aryl portion of arylalkoxycarbonyl, aryloxycarbonyl, arylalkyl, $-\text{OC}(\text{O})\text{NH}(\text{CH}_2)_n\text{aryl}$, arylalkoxy, $-\text{OC}(\text{O})\text{N}(\text{alkyl})(\text{CH}_2)_n\text{aryl}$, and arylthioalkoxy, is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, alkyl, haloalkyl, or haloalkoxy,

wherein n is 0, 1, 2, 3, 4, 5, or 6; or R_4 is H, alkyl substituted with one group that is CO_2H , $-\text{CO}_2-$, $(\text{C}_1\text{-C}_6)\text{alkyl}$, $-\text{C}(\text{O})\text{NRR}$, $-\text{N}(\text{R}_{30})\text{C}(\text{O})\text{NRR}$, $-\text{N}(\text{R}_{30})\text{C}(\text{O})-(\text{C}_1\text{-C}_6)\text{alkoxy}$, or $-\text{NR}_6\text{R}_7$, arylalkoxy, arylalkyl, hydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein

the aryl portion of arylalkoxy, arylalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy; and

R_5 is arylalkyl, alkyl, aryl, alkoxy, heterocycloalkylalkyl, heteroarylalkyl, arylthioalkyl, heterocycloalkyl, or heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, arylalkoxy, thioalkoxy, alkoxycarbonyl, arylalkoxycarbonyl, CO_2H , CN, amidinoxime, NR_6R_7 , $\text{NR}_6\text{R}_7-(\text{C}_1\text{-C}_6\text{ alkyl})-$, $-\text{C}(\text{O})\text{NR}_6\text{R}_7$, amidino, haloalkyl, or haloalkoxy; wherein

R_6 and R_7 are independently at each occurrence H, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_1\text{-C}_6$ alkoxy $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxycarbonyl, OH, $\text{C}_1\text{-C}_6$ hydroxyalkyl, $-(\text{C}_1\text{-C}_4)\text{alkyl}-\text{CO}_2\text{-alkyl}$, pyridyl $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkanoyl, benzyl, phenyl $\text{C}_1\text{-C}_6$ alkoxy, or phenyl $\text{C}_1\text{-C}_6$ alkanoyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are

independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆ alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆ alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂, NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄ alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, thiomorpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A168. Compounds according to embodiment A163 wherein

R₅ is benzyl, phenethyl, phenpropyl, phenbutyl, alkyl, phenyl, alkoxy, pyridyl(C₁-C₆)alkyl, phenyl(C₁-C₆)thioalkyl, pyrrolyl, pyrrolyl(C₁-C₆)alkyl, or pyridyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently (C₁-C₆)alkyl, halogen, (C₁-C₆)alkoxy, phenyl(C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, alkoxycarbonyl, CO₂H, CN, amidinoxime, amidino, CF₃, or OCF₃.

Embodiment A169. Compounds according to embodiment A163 wherein

R₁ is H, Cl, Br, (C₁-C₆)alkyl, carboxaldehyde, hydroxy(C₁-C₆)alkyl,

wherein the alkyl portion of above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy

R₂ is H, phenylthio, -OC(O)NH(CH₂)_naryl, phenylalkyl, -OC(O)N(alkyl)(CH₂)_naryl, or phenylthio(C₁-C₆)alkoxy, wherein n is 1, 2, 3, or 4;

wherein the aryl groups are optionally substituted with
 5 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, C₁-C₄ alkoxy, C₁-C₄ alkyl, CF₃, or OCF₃;

R₃ is bromo, alkoxycarbonyl, phenylalkoxycarbonyl, phenyloxycarbonyl, phenylalkyl, phenylalkoxy, phenyloxy,
 10 phenylthio, thioalkoxy, phenylthioalkoxy, alkenyl, NR₆R₇, or alkyl, wherein

the phenyl portion of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, (C₁-C₄)alkoxy, (C₁-C₄)alkyl,
 15 halo(C₁-C₄)alkyl, or halo(C₁-C₄)alkoxy,

wherein n is 0, 1, 2, 3, or 4;

R₄ is H, alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenylalkoxy, phenylalkyl,
 20 hydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or wherein the phenyl portion of phenylalkoxy, phenylalkyl is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy

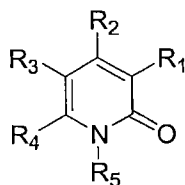
25 R₅ is benzyl, phenethyl, phenpropyl, phenbutyl, alkyl, phenyl, phenyl(C₁-C₆)thioalkyl, pyrrolyl, or pyridyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently (C₁-C₆)alkyl, halogen, (C₁-C₆)alkoxy, benzyloxy, (C₁-C₆)thioalkoxy, alkoxy, alkoxyalkyl, CO₂H, CN, amidinoxime, amidino, CF₃, or OCF₃;

R₆ and R₇ are independently hydrogen, OH, C₁-C₄ alkoxy, C₁-C₆ alkanoyl, or C₁-C₆ alkyl, wherein each of the

above is optionally substituted with 1 or 2 groups that are independently OH, NH₂, C₃-C₆ cycloalkyl, or halogen; or

R₆, R₇, and the nitrogen to which they are attached form a morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl ring which is optionally substituted with 1 or 2 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, hydroxy C₁-C₄ alkyl, or halogen.

Embodiment A170. Compounds according to embodiment 1



or a pharmaceutically acceptable salt thereof, wherein

R₁ is H, halogen, alkyl, carboxaldehyde, hydroxyalkyl, arylalkoxy, arylalkyl, CN, alkanoyl, alkoxy, alkoxyalkyl, or arylalkanoyl,

wherein the aryl portion of arylalkoxy, arylalkyl, and arylalkanoyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, haloalkyl, haloalkoxy or CO₂H;

wherein the alkyl portion of the alkyl, hydroxyalkyl, arylalkoxy, arylalkyl, alkanoyl, alkoxy, alkoxyalkyl and arylalkanoyl groups is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, ethoxy or spirocyclopropyl;

R₂ is arylalkoxy, aryloxy, aryloxyalkyl, OH, halogen, arylthioalkoxy, alkoxy, -OC(O)NH(CH₂)_naryl,

-OC(O)N(alkyl)(CH₂)_naryl, alkyl, alkoxyalkoxy,
dialkylamino, or CO₂H, wherein

n is 0, 1, 2, 3, 4, 5 or 6;

the aryl portion of arylalkoxy, aryloxy, arylthioalkoxy,

5 -OC(O)NH(CH₂)_naryl, and -OC(O)N(alkyl)(CH₂)_naryl or
the heteroaryl and heterocycloalkyl groups is
unsubstituted or substituted with 1, 2, 3, 4, or 5
groups that are independently halogen, -(C₁-C₆)alkyl-
N(R)-CO₂R₃₀, haloalkyl, heteroaryl, heteroarylalkyl,
10 NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -OC(O)NR₆R₇, wherein

R₆ and R₇ are independently at each occurrence H, C₁-C₆
alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₁-C₆
alkoxycarbonyl, OH, C₁-C₆ hydroxyalkyl, -(C₁-C₄)alkyl-
CO₂-alkyl, pyridyl C₁-C₆ alkyl, C₁-C₆ alkanoyl,
15 benzyl, phenyl C₁-C₆ alkoxy, or phenyl C₁-C₆ alkanoyl,
wherein each of the above is unsubstituted or
substituted with 1, 2, or 3 groups that are
independently, halogen, C₃-C₆ cycloalkyl, C₁-C₆
alkoxy, piperidinyl C₁-C₆ alkyl, morpholinyl C₁-C₆
20 alkyl, piperazinyl C₁-C₆ alkyl, OH, SH, NH₂,
NH(alkyl), N(alkyl)(alkyl), -O-C₁-C₄ alkanoyl, C₁-C₄
alkyl, CF₃, or OCF₃; or

R₆, R₇, and the nitrogen to which they are attached form a
morpholinyl, thiomorpholinyl, piperidinyl,
25 pyrrolidinyl, or piperazinyl ring which is
optionally substituted with 1 or 2 groups that are
independently C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy,
hydroxy C₁-C₄ alkyl, or halogen;

R at each occurrence is independently H or C₁-C₆ alkyl;

30 R₃₀ is C₁-C₆ alkyl optionally substituted with 1 or 2
groups that are independently OH, SH, halogen,
amino, monoalkylamino, dialkylamino or C₃-C₆
cycloalkyl;

R₃ is halogen, alkoxycarbonyl, arylalkoxycarbonyl, aryloxycarbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl, arylalkoxy, -OC(O)N(alkyl)(CH₂)_naryl, aryloxy, arylthio, thioalkoxy, arylthioalkoxy, alkenyl, NR₆R₇, C₁-C₆ alkyl, NR₆R₇ or alkyl, wherein

the aryl portion of arylalkoxycarbonyl, aryloxycarbonyl, arylalkyl, -OC(O)NH(CH₂)_naryl, arylalkoxy, -OC(O)N(alkyl)(CH₂)_naryl, and arylthioalkoxy, is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, alkyl, haloalkyl, or haloalkoxy, wherein n is 0, 1, 2, 3, 4, 5, or 6; or

R₄ is H, alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, arylalkoxy, arylalkyl, hydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein the aryl portion of arylalkoxy, arylalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy; and

R₅ is aryl, heterocycloalkylalkyl, heteroarylalkyl, arylthioalkyl, heterocycloalkyl, or heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, halogen, alkoxy, arylalkoxy, thioalkoxy, alkoxycarbonyl, arylalkoxycarbonyl, CO₂H, CN, amidinoxime, NR₆R₇, NR₆R₇-(C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, haloalkyl, or haloalkoxy.

Embodiment A173. Compounds according to embodiment A170 wherein

R₁ is H, halogen, alkyl, carboxaldehyde, hydroxyalkyl, benzyloxy, phenethyloxy, phenpropyloxy, benzyl, phenethyl, phenpropyl, CN, alkanoyl, alkoxy, or phenylC(O)-, phenylCH₂C(O)-, or phenylCH₂CH₂C(O),

5 wherein the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, CN, CF₃, OCF₃ or CO₂H;

10 wherein the above alkyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, methoxy, or ethoxy;

R₂ is benzyloxy, phenethyloxy, phenpropyloxy, phenyloxy, phenyloxy(C₁-C₆)alkyl, OH, halogen, phenylthioalkoxy, alkyl, alkoxy, -OC(O)NH(CH₂)_nphenyl, -
15 OC(O)N(alkyl)(CH₂)_nphenyl, dialkylamino, or CO₂H, wherein n is 0, 1, 2, 3, or 4;

the above aryl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, -(C₁-C₆)alkyl-N(R)-CO₂R₃₀, CF₃, pyridyl, thienyl, NR₆R₇, or NR₆R₇-(C₁-C₆ alkyl)-, wherein
20 R₆ and R₇ are independently at each occurrence H,

alkyl, alkanoyl, benzyl, or phenylC(O)-, wherein the phenyl portion of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, C₃-
25 C₆ cycloalkyl, alkoxy, alkyl, CF₃, or OCF₃;

R₃ is halogen, alkoxycarbonyl, phenylalkoxycarbonyl, phenyloxycarbonyl, phenylalkyl, -OC(O)NH(CH₂)_nphenyl, phenylalkoxy, -OC(O)N(alkyl)(CH₂)_nphenyl, phenyloxy, phenylthio, thioalkoxy, phenylthioalkoxy, alkenyl, NR₆R₇
30 or alkyl, wherein

the phenyl portion of the above is unsubstituted or substituted with 1, 2, or 3 groups that are

independently, halogen, alkoxy, alkyl, haloalkyl, or haloalkoxy,

wherein n is 0, 1, 2, 3, or 4;

R₄ is H, alkyl substituted with one group that is CO₂H, -CO₂-
 5 (C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-
 C₆)alkoxy, or -NR₆R₇, phenylalkoxy, phenylalkyl,
 hydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or
 alkoxyalkoxy, wherein

the phenyl portion of the above is unsubstituted or
 10 substituted with 1, 2, or 3 groups that are
 independently halogen, hydroxy, alkoxy, alkyl,
 nitro, haloalkyl, or haloalkoxy; and

R₅ is phenyl, naphthyl, pyrrolylalkyl, piperidinylalkyl
 pyridinylalkyl, pyrimidinylalkyl, phenylthioalkyl,
 15 pyrrolyl, piperidinyl, pyridyl, or thienylalkyl, wherein
 each of the above is unsubstituted or substituted with 1,
 2, or 3 groups that are independently alkyl, halogen,
 alkoxy, phenylalkoxy, thioalkoxy, alkoxycarbonyl,
 phenylalkoxycarbonyl, CO₂H, CN, amidinoxime, NR₆R₇, NR₆R₇-
 20 (C₁-C₆ alkyl)-, -C(O)NR₆R₇, amidino, haloalkyl, or
 haloalkoxy.

Embodiment A174. Compounds according to embodiment
 A173 wherein

25 R₁ is H, halogen, alkyl, carboxaldehyde, hydroxyalkyl,
 benzyloxy, phenethyloxy, benzyl, phenethyl, CN, (C₁-
 C₆)alkanoyl, alkoxy, or phenylC(O)-, or phenylCH₂C(O)-,
 wherein the above phenyl groups are unsubstituted or
 substituted with 1, 2, or 3 groups that are
 30 independently halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy,
 nitro, CN, CF₃, OCF₃ or CO₂H;

R₂ is benzyloxy, phenethyloxy, phenpropyloxy, phenyloxy,
 phenyloxy(C₁-C₆)alkyl, halogen, phenyl(C₁-C₄)thioalkoxy,

-OC(O)NH(CH₂)_nphenyl, -OC(O)N(alkyl)(CH₂)_nphenyl, or dialkylamino, wherein

n is 0, 1, 2, 3, or 4;

the above phenyl groups are unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, CF₃, NR₆R₇, or NR₆R₇-(C₁-C₆ alkyl)-, wherein R₆ and R₇ are independently at each occurrence H, (C₁-C₆)alkyl, acetyl, benzyl, or phenylC(O)-, wherein the phenyl portion of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, OH, cyclopropyl, alkoxy, alkyl, CF₃, or OCF₃;

R₃ is halogen, alkoxycarbonyl, phenylalkoxycarbonyl, phenyloxycarbonyl, phenylalkyl, phenylalkoxy, phenyloxy, phenylthio, thioalkoxy, phenylthioalkoxy, alkenyl, NR₆R₇ or alkyl, wherein

the phenyl portion of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently, halogen, alkoxy, alkyl, haloalkyl, or haloalkoxy,

wherein n is 0, 1, 2, 3, or 4;

R₄ is H, alkyl substituted with one group that is CO₂H, -CO₂-(C₁-C₆)alkyl, -C(O)NRR, -N(R₃₀)C(O)NRR, -N(R₃₀)C(O)-(C₁-C₆)alkoxy, or -NR₆R₇, phenylalkoxy, phenylalkyl, hydroxyalkyl, haloalkyl, alkoxy, alkoxyalkyl, or alkoxyalkoxy, wherein

the phenyl portion of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, hydroxy, alkoxy, alkyl, nitro, haloalkyl, or haloalkoxy; and

R₅ is phenyl, phenyl(C₁-C₄)thioalkyl, pyridyl, or thienyl(C₁-C₄)alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently

(C₁-C₄)alkyl, fluoro, chloro, bromo, (C₁-C₄)alkoxy, CN, amidinooxime, amidino, CF₃, or OCF₃.

Embodiment A175. Compounds according to embodiment
5 A174 wherein

R₅ is substituted with at least one group selected from fluoro, chloro, bromo, and methyl.

10 In another aspect, the invention provides pharmaceutical compositions comprising at least one pharmaceutically acceptable carrier, solvent, adjuvant or excipient and a compound of formula I, embodiment A66, or embodiment A154.

The invention further provides pharmaceutical
15 compositions comprising at least one pharmaceutically acceptable carrier, solvent, adjuvant or excipient and compounds according to any of the preceding embodiments.

As noted above, the invention encompasses methods of treating a TNF mediated disorder, a p38 kinase mediated
20 disorder, inflammation and/or arthritis in a subject, the method comprising treating a subject having or susceptible to such disorder or condition with a therapeutically-effective amount of a compound of formula I or embodiment A1.

More specifically, the invention provides methods for
25 treating or preventing inflammation; arthritis, rheumatoid arthritis, spondylarthropathies, gouty arthritis, osteoarthritis, systemic lupus erthematosus, juvenile arthritis, and other arthritic conditions; neuroinflammation; allergy, Th2 mediated diseases; pain, neuropathic pain; fever;
30 pulmonary disorders, lung inflammation, adult respiratory distress syndrome, pulmonary sarcoisosis, asthma, silicosis, chronic pulmonary inflammatory disease, and chronic obstructive pulmonary disease (COPD); cardiovascular disease,

arteriosclerosis, myocardial infarction (including post-myocardial infarction indications), thrombosis, congestive heart failure, cardiac reperfusion injury, as well as complications associated with hypertension and/or heart failure such as vascular organ damage, restenosis; cardiomyopathy; stroke including ischemic and hemorrhagic stroke; reperfusion injury; renal reperfusion injury; ischemia including stroke and brain ischemia, and ischemia resulting from cardiac/coronary bypass; neurotrauma and brain trauma including closed head injury; brain edema; neurodegenerative disorders; liver disease and nephritis; gastrointestinal conditions, inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis; ulcerative diseases, gastric ulcers; ophthalmic diseases, retinitis, retinopathies, uveitis, ocular photophobia, acute injury to the eye tissue and ocular traumas such as post-traumatic glaucoma, traumatic optic neuropathy, and central retinal artery occlusion (CRAO); periodontal disease; ophthalmological conditions, retinitis, retinopathies (including diabetic retinopathy), uveitis, ocular photophobia, nonglaucomatous optic nerve atrophy, and age related macular degeneration (ARMD) (including ARMD-atrophic form), corneal graft rejection, ocular neovascularization, retinal neovascularization, neovascularization following injury or infection, retrolental fibroplasias, neovascular glaucoma; glaucoma including primary open angle glaucoma (POAG), juvenile onset primary open-angle glaucoma, angle-closure glaucoma, pseudoexfoliative glaucoma, anterior ischemic optic neuropathy (AION), ocular hypertension, Reiger's syndrome, normal tension glaucoma, neovascular glaucoma, ocular inflammation and corticosteroid-induced glaucoma; diabetes; diabetic nephropathy; skin-related conditions, psoriasis, eczema, burns, dermatitis, keloid formation, scar tissue

formation, angiogenic disorders; viral and bacterial infections, sepsis, septic shock, gram negative sepsis, malaria, meningitis, HIV infection, opportunistic infections, cachexia secondary to infection or malignancy, cachexia
5 secondary to acquired immune deficiency syndrome (AIDS), AIDS, ARC (AIDS related complex), pneumonia, herpes virus; myalgias due to infection; influenza; endotoxic shock; toxic shock syndrome; autoimmune disease, graft vs. host reaction and allograft rejections; treatment of bone resorption diseases,
10 osteoporosis; multiple sclerosis; disorders of the female reproductive system, endometriosis; hemangiomas, infantile hemangiomas, angiofibroma of the nasopharynx, avascular necrosis of bone; benign and malignant tumors/neoplasia, cancer, colorectal cancer, brain cancer, bone cancer,
15 epithelial cell-derived neoplasia (epithelial carcinoma), basal cell carcinoma, adenocarcinoma, gastrointestinal cancer, lip cancer, mouth cancer, esophageal cancer, small bowel cancer, stomach cancer, colon cancer, liver cancer, bladder cancer, pancreas cancer, ovarian cancer, cervical cancer, lung
20 cancer, breast cancer, skin cancer, squamous cell and/or basal cell cancers, prostate cancer, renal cell carcinoma, and other known cancers that affect epithelial cells throughout the body; leukemia; lymphoma; systemic lupus erythematosus (SLE); angiogenesis including neoplasia; metastasis; central nervous
25 system disorders, central nervous system disorders having an inflammatory or apoptotic component, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, spinal cord injury, and peripheral neuropathy; Canine B-Cell Lymphoma. Compounds of the invention are also
30 useful for preventing the production or expression of cyclooxygenase-2, or cyclooxygenase-2 activity.

In this aspect, the invention encompasses methods of treating a p38 kinase or TNF-alpha mediated disorder

comprising administering to a patient in need thereof a therapeutically effective amount of Compounds according to embodiment 1 and at least one pharmaceutically acceptable carrier, adjuvant, solvent or excipient.

- 5 Representative compounds of the invention are:
- 1-benzyl-4-(benzyloxy)-3-bromopyridin-2(1H)-one;
3-bromo-1-(4-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-dimethylphenyl)-6-methylpyridin-2(1H)-one;
10 4-(benzyloxy)-3-bromo-1-(4-fluorobenzyl)pyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(3-fluorobenzyl)pyridin-2(1H)-one;
15 3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;
4-bromo-2-(2,6-dichlorophenyl)-5-[(2,4-difluorobenzyl)oxy]pyridazin-3(2H)-one;
3-bromo-1-(2,6-dichlorophenyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;
20 3-bromo-1-(3-fluorobenzyl)-4-[(3-methylbenzyl)oxy]pyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;
25 4-(benzyloxy)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one;
1-benzyl-4-(benzyloxy)-3-bromo-6-methylpyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-methoxy-6-methylphenyl)-6-methylpyridin-2(1H)-one;
30 3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-fluorobenzyl)pyridin-2(1H)-one;
3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-methylbenzyl)pyridin-2(1H)-one;

5 4-(benzyloxy)-3-bromo-1-(4-chlorobenzyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(3-methoxybenzyl)pyridin-2(1H)-one;

10 4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzoic acid;

4-(benzyloxy)-3-bromo-1-(2-fluorobenzyl)pyridin-2(1H)-one;

3-bromo-1-(2,6-dimethylphenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

15 4-(benzyloxy)-3-bromo-1-[4-(methylthio)benzyl]pyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3-chloropyridin-2(1H)-one;

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}-N'-hydroxybenzenecarboximidamide;

20 methyl 4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzoate;

3-bromo-4-[(3-chlorobenzyl)oxy]-1-(3-fluorobenzyl)pyridin-2(1H)-one;

25 3-bromo-1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;

4-(benzyloxy)-3-bromo-1-(2,6-dichlorophenyl)-6-methylpyridin-2(1H)-one;

30 3-bromo-4-[(4-fluorobenzyl)oxy]-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-bromobenzyl)pyridin-2(1H)-one;

4-{[3-bromo-4-[(4-fluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;

1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]-3-iodopyridin-2(1H)-one;

5 4-bromo-2-(2,6-dichlorophenyl)-5-{[2-(hydroxymethyl)benzyl]oxy}pyridazin-3(2H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

10 3-bromo-1-(2,4-difluorobenzyl)-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-2-ylmethyl)pyridin-2(1H)-one; or a pharmaceutically acceptable salt thereof.

15 Embodiment 57. Compounds according to embodiment 1 or embodiment A1, which is

3-bromo-4-[(4-chlorobenzyl)oxy]-1-(4-fluorobenzyl)pyridin-2(1H)-one;

20 1-benzyl-3-bromo-4-[(4-chlorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(4-chlorobenzyl)-4-[(4-chlorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-4-[(4-chlorobenzyl)oxy]-1-[2-(phenylthio)ethyl]pyridin-2(1H)-one;

25 3-bromo-4-[(4-chlorobenzyl)oxy]-1-(2-phenylethyl)pyridin-2(1H)-one;

3-bromo-4-hydroxy-1-(4-hydroxybenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(piperidin-3-ylmethyl)pyridin-2(1H)-one hydrochloride;

30 3-bromo-1-(4-methoxybenzyl)-4-phenoxy-pyridin-2(1H)-one;

1-benzyl-2-oxo-4-phenoxy-1,2-dihydropyridine-3-carbaldehyde;

3-bromo-4-[(4-chlorobenzyl)oxy]-1-(4-methoxybenzyl)pyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-1-(3-phenylpropyl)pyridin-2(1H)-one;

5 4-(benzyloxy)-1-[4-(benzyloxy)benzyl]-3-bromopyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-[2-(trifluoromethyl)benzyl]pyridin-2(1H)-one;

10 4-(benzyloxy)-3-bromo-1-[3-(trifluoromethyl)benzyl]pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(piperidin-4-ylmethyl)pyridin-2(1H)-one hydrochloride;

1-benzyl-3-bromo-4-{[2-(trifluoromethyl)benzyl]oxy}pyridin-2(1H)-one;

15 1-benzyl-4-[(2,6-dichlorobenzyl)oxy]pyridin-2(1H)-one;
1-benzyl-4-(benzyloxy)-3-(hydroxymethyl)pyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(2,6-dichlorobenzyl)oxy]pyridin-2(1H)-one;

20 1-benzyl-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

25 1-benzyl-3-bromo-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-ethylpyridin-2(1H)-one;

4-(benzyloxy)-1-(4-bromobenzyl)pyridin-2(1H)-one;

3-bromo-1-(4-methylbenzyl)-4-[(4-methylbenzyl)oxy]pyridin-2(1H)-one;

30 methyl 4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzoate;

4-(benzyloxy)-3-bromo-1-(2-thien-3-ylethyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(2-thien-2-ylethyl)pyridin-2(1H)-one;

1-benzyl-4-[(3-chlorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(4-fluorobenzyl)-4-[(4-

5 fluorobenzyl)oxy]pyridin-2(1H)-one;

4-(benzyloxy)-1-(3-fluorobenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-1-(2-fluorobenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one

hydrobromide;

10 4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one;

3-bromo-1-(3-chlorobenzyl)-4-[(4-

chlorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(3-chlorobenzyl)-4-[(4-

fluorobenzyl)oxy]pyridin-2(1H)-one;

15 4-(benzyloxy)-1-(4-chlorobenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-[4-

(trifluoromethoxy)benzyl]pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-tert-butylbenzyl)pyridin-

2(1H)-one;

20 1-benzyl-4-(benzyloxy)-6-methylpyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3,5-dibromo-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-[4-

(trifluoromethyl)benzyl]pyridin-2(1H)-one;

25 1-benzyl-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one;

1-(2-bromobenzyl)-3-[(2-bromobenzyl)oxy]pyridin-2(1H)-one;

methyl 5-chloro-1-(4-chlorobenzyl)-6-oxo-1,6-

dihydropyridine-3-carboxylate;

30 3-benzyl-4-hydroxy-1-(2-phenylethyl)pyridin-2(1H)-one;

5-bromo-1-(2-chloro-6-fluorobenzyl)-3-methylpyridin-2(1H)-one;

1- (2-bromobenzyl) -3- [(2-bromobenzyl) oxy]pyridin-2 (1H) -
one;

1-benzyl-4- (benzyloxy) pyridin-2 (1H) -one;

1-benzyl-4- (benzyloxy) -3-bromopyridin-2 (1H) -one;

5 1-benzyl-4- (benzyloxy) -2-oxo-1,2-dihydropyridine-3-
carbaldehyde;

1-benzyl-4-chloro-2-oxo-1,2-dihydropyridine-3-
carbaldehyde;

10 1-benzyl-4-hydroxy-2-oxo-1,2-dihydropyridine-3-
carbaldehyde;

1-benzyl-4- (benzyloxy) -3-methylpyridin-2 (1H) -one;

4- (benzyloxy) -1- (4-fluorobenzyl) pyridin-2 (1H) -one;

1-benzyl-4- (benzyloxy) -3,5-dibromopyridin-2 (1H) -one;

15 4- (benzyloxy) -3-bromo-1- [4- (methylthio) benzyl] pyridin-
2 (1H) -one;

4- (benzyloxy) -3-bromo-1- (4-fluorobenzyl) pyridin-2 (1H) -
one;

1-benzyl-4- (benzyloxy) -3-chloropyridin-2 (1H) -one;

20 3-bromo-1- (4-fluorobenzyl) -4- [(4-
fluorobenzyl) oxy] pyridin-2 (1H) -one;

1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-4-yl
methyl (phenyl) carbamate;

1-benzyl-3-bromo-4- (2-phenylethyl) pyridin-2 (1H) -one;

1-benzyl-3-bromo-4- (3-phenylpropyl) pyridin-2 (1H) -one;

25 1-benzyl-3-methyl-4- (2-phenylethyl) pyridin-2 (1H) -one;

1-benzyl-3-methyl-4- (3-phenylpropyl) pyridin-2 (1H) -one;

1-benzyl-4- (benzylthio) -3-methylpyridin-2 (1H) -one;

1-benzyl-4- (benzylthio) -3-bromopyridin-2 (1H) -one;

1-benzyl-2-oxo-1,2-dihydropyridin-4-yl methanesulfonate;

30 3-acetyl-4-hydroxy-6-methyl-1- [choro] phenylpyridin-2 (1H) -
one;

6- (benzyloxy) -1-methyl-2-oxo-1,2-dihydropyridine-3-
carbonitrile;

3-benzoyl-6-(benzyloxy)-1-methylpyridin-2(1H)-one;
3-benzyl-6-(benzyloxy)-1-methylpyridin-2(1H)-one;
1-benzyl-4-hydroxypyridin-2(1H)-one;
1-benzyl-4-(benzylthio)pyridin-2(1H)-one
5 4-amino-1-benzylpyridin-2(1H)-one;
1-benzyl-4-(benzyloxy)pyridin-2(1H)-one;
1-benzyl-4-hydroxypyridin-2(1H)-one;
1-benzyl-2-oxo-1,2-dihydropyridin-4-yl
methyl(phenyl) carbamate;
10 or a pharmaceutically acceptable thereof.

Embodiment 58. Compounds according to embodiment 1 or
embodiment A1, which is

4-(benzyloxy)-1-(4-methylbenzyl)pyridin-2(1H)-one;
15 4-(benzyloxy)-3-bromopyridin-2(1H)-one;
methyl 4-{[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]methyl}
benzoate;
methyl-4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-
yl]methyl} benzoate;
20 4-{[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]methyl}
benzonitrile;
4-(benzyloxy)-1-(4-tert-butylbenzyl)pyridin-2(1H)-one;
4-(benzyloxy)-1-[4-(trifluoromethyl)benzyl]pyridin-2(1H)-
one;
25 4-(benzyloxy)-3-bromo-1-[4-(trifluoromethyl)
benzyl]pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-[3-(trifluoromethyl)
benzyl]pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-[2-(trifluoromethyl)
30 benzyl]pyridin-2(1H)-one;
4-(benzyloxy)-1-[4-(trifluoromethoxy)benzyl]pyridin-
2(1H)-one;

4-(benzyloxy)-3-bromo-1-[4-(trifluoromethoxy)
benzyl]pyridin-2(1H)-one;

1-benzyl-4-hydroxy-6-methylpyridin-2(1H)-one;

1-benzyl-6-methyl-2-oxo-1,2-dihydropyridin-4-yl 4-

5 bromobenzenesulfonate;

1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-
2(1H)-one;

1-benzyl-6-methyl-2-oxo-1,2-dihydropyridin-4-yl 4-
bromobenzenesulfonate;

10 1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-
2(1H)-one;

1-Benzyl-4-[2,6-(dichlorobenzyl)oxy]pyridin-2(1H)-one;

4-[(2,6-dichlorobenzyl)oxy]pyridine-1-oxide;

4-[(2,6-dichlorobenzyl)oxy]pyridine 1-oxide;

15 1-Benzyl-3-bromo-4-[2,6-(dichlorobenzyl)oxy]pyridin-
2(1H)-one;

1-Benzyl-3-bromo-4-[(4-methylbenzyl)oxy]pyridin-2(1H)-
one;

1-Benzyl-4-[benzylthio]-3-bromopyridin-2(1H)-one;

20 1-benzyl-4-(benzyloxy)-3-iodopyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3-vinylpyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3-ethylpyridin-2(1H)-one;

3-acetyl-4-(benzyloxy)-1-(2-chlorophenyl)-6-
methylpyridin-2(1H)-one;

25 3-acetyl-1-(2-chlorophenyl)-4-hydroxy-6-methylpyridin-
2(1H)-one;

1-benzyl-3-bromo-4-hydroxypyridin-2(1H)-one;

1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-4-yl
trifluoromethanesulfonate;

30 1-benzyl-3-bromo-4-(phenylethynyl)pyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-6-methyl-4-(2-
phenylethyl)pyridin-2(1H)-one;

1-(3-fluorobenzyl)-4-hydroxy-6-methylpyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-hydroxy-6-methylpyridin-
2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-6-methyl-2-oxo-1,2-
dihydropyridin-4-yl trifluoromethanesulfonate;

5 3-bromo-1-(3-fluorobenzyl)-6-methyl-4-
(phenylethynyl)pyridin-2(1H)-one;

3-acetyl-1-(2,6-dichlorophenyl)-4-hydroxy-6-
methylpyridin-2(1H)-one;

10 1-(2,6-dichlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-
one;

4-(benzyloxy)-1-(2,6-dichlorophenyl)-6-methylpyridin-
2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-(2-phenylethyl)pyridin-
2(1H)-one;

15 3-bromo-1-(3-fluorobenzyl)-4-hydroxypyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl
trifluoromethanesulfonate;

3-bromo-1-(3-fluorobenzyl)-4-(phenylethynyl)pyridin-
2(1H)-one;

20 4-(benzyloxy)-3-ethynyl-1-(3-fluorobenzyl)pyridin-2(1H)-
one;

4-(benzyloxy)-1-(3-fluorobenzyl)-3-iodopyridin-2(1H)-one;

4-(benzyloxy)-1-(3-fluorobenzyl)-3-
[(trimethylsilyl)ethynyl]pyridin-2(1H)-one;

25 4-(benzylamino)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-
one;

1-(3-fluorobenzyl)-4-hydroxypyridin-2(1H)-one;

4-(benzylamino)-1-(3-fluorobenzyl)pyridin-2(1H)-one;

or a pharmaceutically acceptable salt thereof.

30

Embodiment 59. Compounds according to embodiment 1 or
embodiment A1, which is

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-fluorobenzyl)pyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

5 3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

10 3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(3-methoxybenzyl)pyridin-2(1H)-one;

3-bromo-1-(2,6-dimethylphenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-bromo-4-[(3-chlorobenzyl)oxy]-1-(3-fluorobenzyl)pyridin-2(1H)-one;

15 3-bromo-4-[(4-fluorobenzyl)oxy]-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

20 4-{[3-bromo-4-[(4-fluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;

1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]-3-iodopyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

25 3-bromo-1-(2,4-difluorobenzyl)-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-2-ylmethyl)pyridin-2(1H)-one;

30 3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(3-fluorobenzyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-[(3-methylbenzyl)oxy]piperidin-2-one;

5 3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-methoxy-6-methylphenyl)-6-methylpyridin-2(1H)-one;

or a pharmaceutically acceptable salt thereof.

10

Embodiment 60. Compounds according to embodiment 1, which is

1-(1-acetyl-2,3-dihydro-1H-indol-5-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1-glycoloyl-2,3-dihydro-1H-indol-5-yl)-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-indol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(N-methylglycyl)-2,3-dihydro-1H-indol-5-yl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-2,3-dihydro-1H-indol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-indol-5-yl]-6-methylpyridin-2(1H)-one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]indoline-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(methylsulfonyl)-2,3-dihydro-1H-indol-5-yl]pyridin-2(1H)-one;

1-(1-acetyl-1H-indol-5-yl)-3-chloro-4-[(2,4-

difluorobenzyl) oxy] -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- (1-glycoloyl-1H-indol-5-yl) -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [1- (2-hydroxy-2-methylpropanoyl) -1H-indol-5-yl] -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -6-methyl-1- [1- (N-methylglycyl) -1H-indol-5-yl] pyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [1- (3-hydroxypropanoyl) -1H-indol-5-yl] -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [1- (3-hydroxy-3-methylbutanoyl) -1H-indol-5-yl] -6-methylpyridin-2 (1H) -one;

5- [3-chloro-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-oxopyridin-1 (2H) -yl] -1H-indole-1-carboxamide;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -6-methyl-1- [1- (methylsulfonyl) -1H-indol-5-yl] pyridin-2 (1H) -one;

1- (2-acetyl-2,3-dihydro-1H-isoindol-5-yl) -3-chloro-4- [(2,4-difluorobenzyl) oxy] -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- (2-glycoloyl-2,3-dihydro-1H-isoindol-5-yl) -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [2- (2-hydroxy-2-methylpropanoyl) -2,3-dihydro-1H-isoindol-5-yl] -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -6-methyl-1- [2- (N-methylglycyl) -2,3-dihydro-1H-isoindol-5-yl] pyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [2- (3-hydroxypropanoyl) -2,3-dihydro-1H-isoindol-5-yl] -6-methylpyridin-2 (1H) -one;

3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [2- (3-hydroxy-3-methylbutanoyl) -2,3-dihydro-1H-isoindol-5-yl] -6-methylpyridin-2 (1H) -one;

5- [3-chloro-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-oxopyridin-1 (2H) -yl] -1,3-dihydro-2H-isoindole-2-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(methylsulfonyl)-2,3-dihydro-1*H*-isoindol-5-yl]pyridin-2(1*H*)-one;

1-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-6-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2-glycoloyl-1,2,3,4-tetrahydroisoquinolin-6-yl)-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2-(2-hydroxy-2-methylpropanoyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(*N*-methylglycyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2-(3-hydroxypropanoyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2-(3-hydroxy-3-methylbutanoyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]-6-methylpyridin-2(1*H*)-one;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2*H*)-yl]-3,4-dihydroisoquinoline-2(1*H*)-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]pyridin-2(1*H*)-one;

1-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2-glycoloyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2-(2-hydroxy-2-methylpropanoyl)-1,2,3,4-tetrahydroisoquinolin-7-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(*N*-methylglycyl)-1,2,3,4-tetrahydroisoquinolin-7-yl]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2-(3-hydroxypropanoyl)-1,2,3,4-tetrahydroisoquinolin-7-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2-(3-hydroxy-3-methylbutanoyl)-1,2,3,4-tetrahydroisoquinolin-7-yl]-6-methylpyridin-2(1*H*)-one;

7-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2*H*)-yl]-3,4-dihydroisoquinoline-2(1*H*)-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-7-yl]pyridin-2(1*H*)-one;

1-(1-acetyl-1*H*-benzimidazol-5-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1-glycoloyl-1*H*-benzimidazol-5-yl)-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-1*H*-benzimidazol-5-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(*N*-methylglycyl)-1*H*-benzimidazol-5-yl]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-1*H*-benzimidazol-5-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-1*H*-benzimidazol-5-yl]-6-methylpyridin-2(1*H*)-one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2*H*)-yl]-1*H*-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(methylsulfonyl)-1*H*-benzimidazol-5-yl]pyridin-2(1*H*)-one;

3-chloro-1-(1,3-diacetyl-2,3-dihydro-1*H*-benzimidazol-5-yl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

1-(3-acetyl-1-glycoloyl-2,3-dihydro-1*H*-benzimidazol-5-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

1-[3-acetyl-1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1*H*-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

1-[3-acetyl-1-(*N*-methylglycyl)-2,3-dihydro-1*H*-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

1-[3-acetyl-1-(3-hydroxypropanoyl)-2,3-dihydro-1*H*-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

1-[3-acetyl-1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1*H*-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

3-acetyl-5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2*H*)-yl]-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

1-(1-acetyl-3-glycoloyl-2,3-dihydro-1*H*-benzimidazol-5-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1,3-diglycoloyl-2,3-dihydro-1*H*-benzimidazol-5-yl)-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-glycoloyl-1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1*H*-benzimidazol-5-yl]-6-methylpyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-glycoloyl-1-(*N*-methylglycyl)-2,3-dihydro-1*H*-benzimidazol-5-yl]-6-

methylpyridin-2 (1H) -one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-glycoloyl-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-

methylpyridin-2 (1H) -one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1 (2H) -yl]-3-glycoloyl-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-glycoloyl-1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2 (1H) -one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-glycoloyl-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2 (1H) -one;

1-[1-acetyl-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2 (1H) -one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-glycoloyl-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2 (1H) -one;

1-[1,3-bis(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2 (1H) -one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(2-hydroxy-2-methylpropanoyl)-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2 (1H) -one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(2-hydroxy-2-methylpropanoyl)-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2 (1H) -one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2 (1H) -one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxopyridin-1(2H)-yl]-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(2-hydroxy-2-methylpropanoyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

1-[1-acetyl-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-glycoloyl-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

1-[1,3-bis(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[3-(N-methylglycyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2(1H)-one;

1-[1-acetyl-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-glycoloyl-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(3-hydroxypropanoyl)-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

1-[1,3-bis(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(3-hydroxypropanoyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

1-[1-acetyl-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-glycoloyl-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(3-hydroxy-3-methylbutanoyl)-1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(3-hydroxy-3-methylbutanoyl)-1-(N-methylglycyl)-2,3-dihydro-1H-

benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(3-hydroxy-3-methylbutanoyl)-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

1-[1,3-bis(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[3-(3-hydroxy-3-methylbutanoyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-acetyl-6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-glycoloyl-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxopyridin-1(2H)-yl]-1H-benzimidazole-1,3(2H)-dicarboxamide;

6-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

1-[1-acetyl-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-glycoloyl-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(N-methylglycyl)-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylpyridin-2(1H)-one;

5-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

1-[1,3-bis(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-[3-acetyl-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-(1-acetyl-1H-pyrrol-3-yl)-3-chloro-4-[(2,4-

difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1-glycoloyl-1H-pyrrol-3-yl)-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-1H-pyrrol-3-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(N-methylglycyl)-1H-pyrrol-3-yl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-1H-pyrrol-3-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-1H-pyrrol-3-yl]-6-methylpyridin-2(1H)-one;

3-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-1H-pyrrole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(methylsulfonyl)-1H-pyrrol-3-yl]pyridin-2(1H)-one;

1-(1-acetyl-1H-imidazol-4-yl)-3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1-glycoloyl-1H-imidazol-4-yl)-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-1H-imidazol-4-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(N-methylglycyl)-1H-imidazol-4-yl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-1H-imidazol-4-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-1H-imidazol-4-yl]-6-methylpyridin-2(1H)-one;

4-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-1H-imidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(methylsulfonyl)-1H-imidazol-4-yl]pyridin-2(1H)-one;

1-(1-acetyl-1H-pyrazol-4-yl)-3-chloro-4-[(2,4-

difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1-glycoloyl-1H-pyrazol-4-yl)-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(2-hydroxy-2-methylpropanoyl)-1H-pyrazol-4-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(N-methylglycyl)-1H-pyrazol-4-yl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxypropanoyl)-1H-pyrazol-4-yl]-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[1-(3-hydroxy-3-methylbutanoyl)-1H-pyrazol-4-yl]-6-methylpyridin-2(1H)-one;

4-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-1H-pyrazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[1-(methylsulfonyl)-1H-pyrazol-4-yl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-isoquinolin-7-yl-6-methylpyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(isoquinolin-6-ylmethyl)pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-dihydro-2H-indol-2-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2,3-dihydro-1H-indol-5-ylmethyl)pyridin-2(1H)-one;

1-[(1-acetyl-2,3-dihydro-1H-indol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(1-glycoloyl-2,3-dihydro-1H-indol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-indol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(N-methylglycyl)-2,3-dihydro-1H-indol-5-yl]methyl}pyridin-2(1H)-

one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxypropanoyl)-2,3-dihydro-1H-indol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-indol-5-yl]methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}indoline-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(methylsulfonyl)-2,3-dihydro-1H-indol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2,3-dihydro-1H-isoindol-5-ylmethyl)pyridin-2(1H)-one;

1-[(2-acetyl-2,3-dihydro-1H-isoindol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(2-glycoloyl-2,3-dihydro-1H-isoindol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-isoindol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(N-methylglycyl)-2,3-dihydro-1H-isoindol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(3-hydroxypropanoyl)-2,3-dihydro-1H-isoindol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-isoindol-5-yl]methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-dihydro-2H-isoindole-2-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(methylsulfonyl)-2,3-dihydro-1*H*-isoindol-5-yl]methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1,2,3,4-tetrahydroisoquinolin-6-ylmethyl)pyridin-2(1*H*)-one;

1-[(2-acetyl-1,2,3,4-tetrahydroisoquinolin-6-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(2-glycoloyl-1,2,3,4-tetrahydroisoquinolin-6-yl)methyl]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(2-hydroxy-2-methylpropanoyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(*N*-methylglycyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(3-hydroxypropanoyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(3-hydroxy-3-methylbutanoyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]methyl}pyridin-2(1*H*)-one;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxypyridin-1(2*H*)-yl]methyl}-3,4-dihydroisoquinoline-2(1*H*)-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1,2,3,4-tetrahydroisoquinolin-5-ylmethyl)pyridin-2(1*H*)-one;

1-[(2-acetyl-1,2,3,4-tetrahydroisoquinolin-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(2-glycoloyl-1,2,3,4-tetrahydroisoquinolin-5-yl)methyl]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(2-hydroxy-2-methylpropanoyl)-1,2,3,4-tetrahydroisoquinolin-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(N-methylglycyl)-1,2,3,4-tetrahydroisoquinolin-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(3-hydroxypropanoyl)-1,2,3,4-tetrahydroisoquinolin-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(3-hydroxy-3-methylbutanoyl)-1,2,3,4-tetrahydroisoquinolin-5-yl]methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxypyridin-1(2H)-yl]methyl}-3,4-dihydroisoquinoline-2(1H)-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2,3-dihydro-1H-benzimidazol-5-ylmethyl)pyridin-2(1H)-one;

1-[(1-acetyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(1-glycoloyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

1-[(3-acetyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-1-[(1,3-diacetyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

1-[(3-acetyl-1-glycoloyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

1-{[3-acetyl-1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

1-{[3-acetyl-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

1-{[3-acetyl-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

1-{[3-acetyl-1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2,3-dihydro-1H-benzimidazole-1-carboxamide;

1-{[3-acetyl-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-

difluorobenzyl) oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(3-glycoloyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

1-[(1-acetyl-3-glycoloyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[(1,3-diglycoloyl-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-glycoloyl-1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-glycoloyl-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-glycoloyl-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-glycoloyl-1-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl)methyl}-3-glycoloyl-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-glycoloyl-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

1-{[1-acetyl-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-glycoloyl-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

1-{[1,3-bis(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(2-hydroxy-2-methylpropanoyl)-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(2-hydroxy-2-methylpropanoyl)-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxy-3-methylbutanoyl)-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxypyridin-1(2H)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(2-hydroxy-2-methylpropanoyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

1-{[1-acetyl-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-glycoloyl-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(2-hydroxy-2-methylpropanoyl)-3-(N-methylglycyl)-2,3-dihydro-1H-

benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

1-{[1,3-bis(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxypropanoyl)-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxy-3-methylbutanoyl)-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl)methyl}-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(N-methylglycyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

1-{[1-acetyl-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-glycoloyl-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(2-hydroxy-2-methylpropanoyl)-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxypropanoyl)-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}pyridin-2(1H)-one;

1-{[1,3-bis(3-hydroxypropanoyl)-2,3-dihydro-1H-

benzimidazol-5-yl)methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxy-3-methylbutanoyl)-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl)methyl}-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxypropanoyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

1-{[1-acetyl-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-glycoloyl-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxy-3-methylbutanoyl)-1-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxy-3-methylbutanoyl)-1-(N-methylglycyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxy-3-methylbutanoyl)-1-(methylsulfonyl)-2,3-dihydro-1H-benzimidazol-5-yl)methyl]pyridin-2(1H)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl)methyl}-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

1-{[1,3-bis(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-(3-hydroxy-3-methylbutanoyl)-1-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazol-5-yl]methyl}pyridin-2(1H)-one;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-acetyl-6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(N-methylglycyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxypropanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1H-benzimidazole-1,3(2H)-dicarboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(methylsulfonyl)-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[3-

(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}pyridin-2(1*H*)-one;

1-{[1-acetyl-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-glycoloyl-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(2-hydroxy-2-methylpropanoyl)-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(*N*-methylglycyl)-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxypropanoyl)-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}pyridin-2(1*H*)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[1-(3-hydroxy-3-methylbutanoyl)-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}pyridin-2(1*H*)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl)methyl}-3-(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

1-{[1,3-bis(methylsulfonyl)-2,3-dihydro-1*H*-benzimidazol-5-yl)methyl}-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1*H*)-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl)methyl}-1,3-dihydro-2*H*-benzimidazol-2-one;

1-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl)methyl}-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl)methyl}-1-glycoloyl-1,3-dihydro-2*H*-benzimidazol-2-

one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(methylsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-acetyl-6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-dihydro-2H-benzimidazol-2-one;

1,3-diacetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-dihydro-2H-benzimidazol-2-one;

3-acetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-glycoloyl-1,3-dihydro-2H-benzimidazol-2-one;

3-acetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

3-acetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

3-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

3-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

3-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(methanesulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-glycoloyl-1,3-dihydro-2H-benzimidazol-2-one;

1-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-diglycoloyl-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-1-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-1-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-1-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-1-(3-hydroxy-3-methylbutanoyl)-

1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-glycoloyl-2-oxo-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-glycoloyl-1-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

1-acetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-glycoloyl-3-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1,3-bis(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-1-(*N*-methylglycyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-1-(3-hydroxypropanoyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-3-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-2-oxo-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-

1-(2H)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-1-(methylsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-3-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1-glycoloyl-3-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1-(2-hydroxy-2-methylpropanoyl)-3-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1,3-bis(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1-(3-hydroxypropanoyl)-3-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-3-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-3-(N-methylglycyl)-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-3-(N-methylglycyl)-1-(methylsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1-(2H)-yl]methyl}-1-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-acetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-glycoloyl-3-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(2-hydroxy-2-methylpropanoyl)-3-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxypropanoyl)-1-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-bis(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-3-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxypropanoyl)-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxypropanoyl)-1-(methylsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-acetyl-5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1-glycoloyl-3-(3-hydroxy-3-methylbutanoyl)-

1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-1-(2-hydroxy-2-methylpropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-1-(N-methylglycyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-1-(3-hydroxypropanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-bis(3-hydroxy-3-methylbutanoyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-1-(methylsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

3-acetyl-6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-glycoloyl-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(2-hydroxy-2-methylpropanoyl)-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

6-{ [3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-

1(2H)-yl]methyl}-3-(*N*-methylglycyl)-2-oxo-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(3-hydroxypropanoyl)-2-oxo-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(3-hydroxy-3-methylbutanoyl)-2-oxo-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-2-oxo-1*H*-benzimidazole-1,3(2*H*)-dicarboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(methylsulfonyl)-2-oxo-2,3-dihydro-1*H*-benzimidazole-1-carboxamide;

6-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

1-acetyl-5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-3-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-glycoloyl-3-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-(2-hydroxy-2-methylpropanoyl)-3-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-(*N*-methylglycyl)-3-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2*H*)-yl]methyl}-1-(3-hydroxypropanoyl)-3-(methylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-

1(2H)-yl]methyl}-1-(3-hydroxy-3-methylbutanoyl)-3-(methanolsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-3-(methanolsulfonyl)-2-oxo-2,3-dihydro-1H-benzimidazole-1-carboxamide;

5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}-1,3-bis(methanolsulfonyl)-1,3-dihydro-2H-benzimidazol-2-one;

3-benzyl-4-hydroxy-1-(2-phenylethyl)pyridin-2(1H)-one;

1-benzyl-4-hydroxy-2-oxo-1,2-dihydropyridine-3-carbaldehyde;

1-benzyl-4-chloro-2-oxo-1,2-dihydropyridine-3-carbaldehyde;

methyl 5-chloro-1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridine-3-carboxylate;

5-bromo-1-(2-chloro-6-fluorobenzyl)-3-methylpyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(4-fluorophenyl)ethynyl]-6-methylpyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(4-fluorophenyl)ethynyl]-6-methylpyridin-2(1H)-one;

methyl 3-chloro-4-[4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoate;

4-[(2,4-difluorobenzyl)oxy]-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile;

4-[(2,4-difluorobenzyl)oxy]-6-(hydroxymethyl)-1-(2,4,6-trifluorophenyl)pyridin-2(1H)-one;

4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(trifluoromethyl)phenyl]pyridin-2(1H)-one;

3-[4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzaldehyde;

4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluoro-4-morpholin-

4-ylphenyl)-6-methylpyridin-2(1H)-one;

4-[(2,4-difluorobenzyl)oxy]-1-[2,6-difluoro-4-(4-methylpiperazin-1-yl)phenyl]-6-methylpyridin-2(1H)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoic acid;

4-[(2,4-difluorobenzyl)oxy]-1-[4-(dimethylamino)-2,6-difluorophenyl]-6-methylpyridin-2(1H)-one;

4-[(2,4-difluorobenzyl)oxy]-1-{2,6-difluoro-4-[(2-hydroxyethyl)(methyl)amino]phenyl}-6-methylpyridin-2(1H)-one;

methyl 3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoate;

3-[4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-4-methylbenzoic acid;

4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-(hydroxymethyl)pyridin-2(1H)-one;

3-bromo-1-{[5-(chloromethyl)pyrazin-2-yl]methyl}-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-[2-chloro-5-(hydroxymethyl)phenyl]-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluoro-4-hydroxyphenyl)-6-methylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[4-(hydroxymethyl)-2-methoxyphenyl]-6-methylpyridin-2(1H)-one;

methyl 3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-4-methylbenzoate;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}pyridin-2(1H)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-[2-(dimethylamino)ethyl]benzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-(2-methoxyethyl)benzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxopyridin-1(2H)-yl]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-(2-hydroxyethyl)-N-methylbenzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-(2-methoxyethyl)-N-methylbenzamide;

4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzamide;

methyl 3-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-4-fluorobenzoate;

4-[4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-methylbenzoic acid;

1-(4-bromo-2-methylphenyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-[(1-acetyl-1H-indol-5-yl)methyl]-3-chloro-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[(5-methylpyrazin-2-yl)methyl]pyridin-2(1H)-one;

methyl 2-([3-bromo-1-(2,6-difluorophenyl)-6-methyl-2-oxo-1,2-dihydropyridin-4-yl]oxy)methyl)-3,5-difluorobenzylcarbamate;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{[5-(hydroxymethyl)pyrazin-2-yl]methyl}-6-methylpyridin-2(1H)-one;

4-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}-N,N-dimethylbenzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-(2-hydroxyethyl)-4-methylbenzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-{4-[(4-methylpiperazin-1-yl)carbonyl]benzyl}pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1H-indol-5-ylmethyl)pyridin-2(1H)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxypyridin-1 (2H) -yl] -N-methylbenzamide;
3- [3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-oxypyridin-1 (2H) -yl] benzamide;
3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- { [5-(hydroxymethyl) pyrazin-2-yl] methyl} -6-methylpyridin-2 (1H) -one;
3- [3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-oxypyridin-1 (2H) -yl] -N- (2-methoxyethyl) -4-methylbenzamide;
3- [3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-oxypyridin-1 (2H) -yl] -N,4-dimethylbenzamide;
3- [3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-oxypyridin-1 (2H) -yl] -N,N,4-trimethylbenzamide;
3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-1- [2-methyl-5- (morpholin-4-ylcarbonyl) phenyl] pyridin-2 (1H) -one;
3-bromo-4- [(2,4-difluorobenzyl) oxy] -1- [5- (1-hydroxy-1-methylethyl) -2-methylphenyl] -6-methylpyridin-2 (1H) -one;
1- (2-bromobenzyl) -3- [(2-bromobenzyl) oxy] pyridin-2 (1H) -one;
1- (2-bromobenzyl) -3- [(2-bromobenzyl) oxy] pyridin-2 (1H) -one;
3-bromo-1- (4-methoxybenzyl) -4-phenoxy pyridin-2 (1H) -one;
1-benzyl-2-oxo-4-phenoxy-1,2-dihydropyridine-3-carbaldehyde;
3-Bromo-4- (2,4-difluoro-benzyloxy) -1- (3-dimethylaminomethyl-benzyl) -6-methyl-1H-pyridin-2-one;
N- {3- [3-Bromo-4- (2,4-difluoro-benzyloxy) -6-methyl-2-oxo-2H-pyridin-1-ylmethyl] -benzyl} -2-hydroxy-acetamide;
3-Bromo-4- (2,4-difluoro-benzyloxy) -6-methyl-1- [4- (piperidine-1-carbonyl) -benzyl] -1H-pyridin-2-one;
3-bromo-4- [(2,4-difluorobenzyl) oxy] -1- (2,6-difluorophenyl) -6- [(ethoxyamino) methyl] pyridin-2 (1H) -one;
4- [3-Bromo-4- (2,4-difluoro-benzyloxy) -6-methyl-2-oxo-2H-pyridin-1-ylmethyl] -N-isopropyl-benzamide;

N-(3-aminopropyl)-4-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}benzamide hydrochloride;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N,4-dimethylbenzamide;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N,N-bis-(2-hydroxy-ethyl)-benzamide;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-[4-(pyrrolidine-1-carbonyl)-benzyl]-1H-pyridin-2-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-hydroxy-benzamide;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-methyl-benzamide;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-(2-dimethylamino-ethyl)-benzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(1H-indazol-5-ylmethyl)pyridin-2(1H)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-[4-(4-methyl-piperazine-1-carbonyl)-benzyl]-1H-pyridin-2-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-4-methylbenzaldehyde;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(4-dimethylaminomethyl-benzyl)-6-methyl-1H-pyridin-2-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-(2-methoxyethyl)-4-methylbenzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[2-(dimethylamino)-4,6-difluorophenyl]-6-methylpyridin-2(1H)-one hydrochloride;

N-(2-aminoethyl)-4-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}benzamide hydrochloride;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-(2-hydroxy-ethyl)-benzamide;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(4-hydroxymethyl-

benzyl)-6-methyl-1H-pyridin-2-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[2,6-difluoro-4-(4-methylpiperazin-1-yl)phenyl]-6-methylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[2-(dimethylamino)-4,6-difluorophenyl]-6-methylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[2,6-difluoro-4-(4-methylpiperazin-1-yl)phenyl]-6-methylpyridin-2(1H)-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-(2-methoxy-ethyl)-benzamide;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-{4-[(2-hydroxyethylamino)-methyl]-benzyl}-6-methyl-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-[(dimethylamino)methyl]pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-methyl-5-(morpholin-4-ylcarbonyl)phenyl]pyridin-2(1H)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(4-methylaminomethyl-benzyl)-1H-pyridin-2-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-[4-(morpholine-4-carbonyl)-benzyl]-1H-pyridin-2-one;

N-(2-aminoethyl)-3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzamide;

N-(3-aminopropyl)-3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzamide hydrochloride;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-(2-methoxy-ethyl)-N-methyl-benzamide;

1-(4-Aminomethyl-benzyl)-3-bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[4-(piperazin-1-ylcarbonyl)benzyl]pyridin-2(1H)-one hydrochloride;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-[4-(isopropylamino-methyl)-benzyl]-6-methyl-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-dimethylphenyl)-6-methylpyridin-2(1H)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-{3-[(2-hydroxyethylamino)-methyl]-benzyl}-6-methyl-1H-pyridin-2-one;

1-(3-Aminomethyl-benzyl)-3-bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(4-hydroxy-benzyl)-6-methyl-1H-pyridin-2-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-[(dimethylamino)methyl]pyridin-2(1H)-one;

N-{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzyl}-acetamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{2,6-difluoro-4-[(2-hydroxyethyl)(methyl)amino]phenyl}-6-methylpyridin-2(1H)-one;

ethyl 3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoate;

1-[3-(aminomethyl)benzyl]-3-bromo-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one trifluoroacetate;

1-(3-{[Bis-(2-hydroxy-ethyl)-amino]-methyl}-benzyl)-3-bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-[3-(isopropylamino-methyl)-benzyl]-6-methyl-1H-pyridin-2-one;

{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzyl}-carbamic acid tert-butyl ester;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzamide;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-[4-(1-hydroxy-1-methyl-ethyl)-benzyl]-6-methyl-1H-pyridin-2-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(3-dimethylaminomethyl-benzyl)-1H-pyridin-2-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(3-

piperidin-1-ylmethyl-benzyl)-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-{[(2-methoxyethyl)amino]methyl}pyridin-2(1H)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-methylbenzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{2,4-difluoro-6-[(2-hydroxyethyl)(methyl)amino]phenyl}-6-methylpyridin-2(1H)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(3-morpholin-4-ylmethyl-benzyl)-1H-pyridin-2-one;

3-bromo-1-(2,6-dimethylphenyl)-6-methyl-4-[(2,4,6-trifluorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(2,6-dimethylphenyl)-6-methyl-4-[(2,4,6-trifluorobenzyl)oxy]pyridin-2(1H)-one;

1-(4-{[Bis-(2-hydroxy-ethyl)-amino]-methyl}-benzyl)-3-bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluoro-4-morpholin-4-ylphenyl)-6-methylpyridin-2(1H)-one;

4-Benzyloxy-3-bromo-1-(4-fluoro-benzyl)-1H-pyridin-2-one;

4-[3-Chloro-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N,N,4-trimethylbenzamide;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-isopropylbenzamide;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzamide;

3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzonitrile;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(3-piperazin-1-ylmethyl-benzyl)-1H-pyridin-2-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-(2-hydroxy-ethyl)-N-methyl-benzamide;
methyl 4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-3-chlorobenzoate;
3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-[3-(morpholine-4-carbonyl)-benzyl]-1H-pyridin-2-one;
3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N,N-bis-(2-hydroxy-ethyl)-benzamide;
4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzoic acid methyl ester;
3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-hydroxy-benzamide;
3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(3-hydroxymethyl-benzyl)-6-methyl-1H-pyridin-2-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(3-fluorobenzyl)pyridin-2(1H)-one;
3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(3-fluoro-benzyl)-1H-pyridin-2-one;
N-{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzyl}-methanesulfonamide;
3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-[3-(pyrrolidine-1-carbonyl)-benzyl]-1H-pyridin-2-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;
N-(3-aminopropyl)-3-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}benzamide hydrochloride;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;
3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(3-methylaminomethyl-benzyl)-1H-pyridin-2-one;
4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxypyridin-1(2H)-yl]-3,5-dichlorobenzenesulfonamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[4-(dimethylamino)-2,6-difluorophenyl]-6-methylpyridin-2(1H)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(4-piperidin-1-ylmethyl-benzyl)-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

N-(2-aminoethyl)-3-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxypyridin-1(2H)-yl]methyl}benzamide hydrochloride;

3-bromo-1-[2-chloro-5-(hydroxymethyl)phenyl]-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-methylpyridin-2(1H)-one;

3-chloro-1-[2-chloro-5-(hydroxymethyl)phenyl]-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxypyridin-1(2H)-yl]-N-(2-hydroxyethyl)-4-methylbenzamide;

2-{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-phenyl}-acetamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[3-(piperazin-1-ylcarbonyl)benzyl]pyridin-2(1H)-one hydrochloride;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-methylpyridin-2(1H)-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzoic acid methyl ester;

1-(3-Aminomethyl-2-fluoro-benzyl)-3-bromo-4-(2,4-difluoro-benzyloxy)-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-(morpholin-4-ylmethyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-fluorobenzyl)pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1*H*-indol-5-ylmethyl)pyridin-2(1*H*)-one;

1-[3-(aminomethyl)benzyl]-3-bromo-4-[(4-fluorobenzyl)oxy]pyridin-2(1*H*)-one trifluoroacetate;

1-[3-(2-aminoethyl)benzyl]-3-bromo-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1*H*)-one trifluoroacetate;

1-[3-(aminomethyl)benzyl]-3-bromo-4-[(4-fluorobenzyl)oxy]pyridin-2(1*H*)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1*H*)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxypyridin-1(2*H*)-yl]-*N*-(2-hydroxyethyl)benzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1*H*)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(4-methoxy-benzyl)-6-methyl-1*H*-pyridin-2-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2*H*-pyridin-1-ylmethyl]-*N,N*-dimethyl-benzamide;

3-bromo-6-methyl-1-(pyridin-4-ylmethyl)-4-[(2,4,6-trifluorobenzyl)oxy]pyridin-2(1*H*)-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2*H*-pyridin-1-ylmethyl]-benzamide;

3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2*H*-pyridin-1-ylmethyl]-*N*-methyl-benzamide;

{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2*H*-pyridin-1-ylmethyl]-benzyl}-carbamic acid methyl ester;

3-bromo-4-[(2,6-difluorobenzyl)oxy]-1-(2,6-dimethylphenyl)-6-methylpyridin-2(1*H*)-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2*H*-pyridin-1-ylmethyl]-benzonitrile;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1*H*)-one;

1-benzyl-4-(benzyloxy)-3-bromo-6-methylpyridin-2(1H)-one;
1-Benzyl-4-benzyloxy-3-bromo-6-methyl-1H-pyridin-2-one;
1-benzyl-4-(benzyloxy)-3-bromo-6-methylpyridin-2(1H)-one;
1-Benzyl-3-bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;
{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-phenyl}-acetonitrile;
3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-(2-hydroxy-ethyl)-benzamide;
3-Chloro-4-(2,4-difluoro-benzyloxy)-1-(3-fluoro-benzyl)-1H-pyridin-2-one;
1-Allyl-3-chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;
3-Chloro-4-(2,4-difluoro-benzyloxy)-1-[4-(isopropylamino-methyl)-benzyl]-1H-pyridin-2-one;
methyl 3-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-4-methylbenzoate;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-(hydroxymethyl)-1-(2,4,6-trifluorophenyl)pyridin-2(1H)-one;
3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(4-piperazin-1-ylmethyl-benzyl)-1H-pyridin-2-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-(hydroxymethyl)pyridin-2(1H)-one;
3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N,N-dimethyl-benzamide;
3-bromo-1-(3-fluorobenzyl)-4-[(3-methylbenzyl)oxy]pyridin-2(1H)-one;
3-Bromo-1-(3-fluoro-benzyl)-4-(3-methyl-benzyloxy)-1H-pyridin-2-one;
3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(1,2,3,4-tetrahydroisoquinolin-5-ylmethyl)pyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-[(3-

methylbenzyl)oxy]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(isoquinolin-5-ylmethyl)pyridin-2(1H)-one trifluoroacetate;

3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-({5-[(4-methylpiperazin-1-yl)carbonyl]pyrazin-2-yl}methyl)pyridin-2(1H)-one trifluoroacetate;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[5-(hydroxymethyl)-2-methylphenyl]-6-methylpyridin-2(1H)-one;

1-allyl-3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-methoxy-6-methylphenyl)-6-methylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-methoxy-6-methylphenyl)-6-methylpyridin-2(1H)-one;

3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzamide;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-(hydroxymethyl)-1-(2,4,6-trifluorophenyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(trifluoromethyl)phenyl]pyridin-2(1H)-one;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzoic acid;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(4-morpholin-4-ylmethyl-benzyl)-1H-pyridin-2-one;

4-(2,4-Difluoro-benzyloxy)-1-(3-fluoro-benzyl)-3-iodo-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(2,4,6-trifluorophenyl)pyridin-2(1H)-one;

3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-hydroxybenzamide;

3-bromo-1-(2,6-dichlorophenyl)-4-[(2,6-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzonitrile;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[3-(pyrrolidin-1-ylcarbonyl)phenyl]pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2-fluorobenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-methylbenzyl)pyridin-2(1H)-one;

3-{[3-chloro-4-[(2,4-difluorobenzyl)amino]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;

3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-N-isopropyl-benzamide;

3-bromo-1-(4-bromo-2,6-difluorophenyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-chlorobenzyl)pyridin-2(1H)-one;

4-Benzyloxy-3-bromo-1-(4-chloro-benzyl)-1H-pyridin-2-one;

3-bromo-1-(4-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-Bromo-1-(4-fluoro-benzyl)-4-(4-fluoro-benzyloxy)-1H-

pyridin-2-one;

methyl 4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoate;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzoic acid;

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzoic acid;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(2,4,6-trifluorophenyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(2-fluorobenzyl)pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-(hydroxymethyl)pyridin-2(1H)-one;

N-(2-aminoethyl)-4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzamide hydrochloride;

4-Benzyloxy-3-bromo-1-(4-methylsulfanyl-benzyl)-1H-pyridin-2-one;

1-Benzyl-4-benzyloxy-3-chloro-1H-pyridin-2-one;

4-(benzyloxy)-3-bromo-1-[4-(methylthio)benzyl]pyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3-chloropyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{[5-(hydroxymethyl)pyrazin-2-yl]methyl}-6-methylpyridin-2(1H)-one;

3-bromo-1-(2,6-dimethylphenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-bromo-1-(2,6-dimethylphenyl)-4-[(4-fluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-[3-(isopropylamino-methyl)-benzyl]-1H-pyridin-2-one;

3-[3-Chloro-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-2-fluoro-benzamide;

5-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxopyridin-1(2H)-yl)methyl}-N-(2,3-dihydroxypropyl)pyrazine-2-carboxamide;

{3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-phenyl}-acetic acid ethyl ester;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-N-hydroxy-benzamidine;

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl)methyl}-N'-hydroxybenzenecarboximidamide;

ethyl 5-{[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl)methyl}pyrazine-2-carboxylate;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(3-methoxy-benzyl)-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[(5-methylpyrazin-2-yl)methyl]pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(3-methoxybenzyl)pyridin-2(1H)-one;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzoic acid methyl ester;

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(4-dimethylaminomethyl-benzyl)-1H-pyridin-2-one;

3-Chloro-4-(2,4-difluoro-benzyloxy)-1-(3-methanesulfonyl-benzyl)-1H-pyridin-2-one;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzoic acid methyl ester;

methyl 4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl)methyl}benzoate;

ethyl 5-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl)methyl}pyrazine-2-carboxylate;

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl)methyl}benzonitrile;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzonitrile;

{3-[3-Bromo-4-(4-fluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzyl}-carbamic acid tert-butylester;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[5-(1-hydroxy-1-methylethyl)-2-methylphenyl]-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(2,6-dichlorophenyl)-6-methylpyridin-2(1H)-one;

1-(3-Aminomethyl-benzyl)-4-benzyloxy-3-bromo-1H-pyridin-2-one;

3-bromo-4-[(4-fluorobenzyl)oxy]-1-(pyridin-4-ylmethyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(4-bromobenzyl)pyridin-2(1H)-one;

4-Benzyloxy-3-bromo-1-(4-bromo-benzyl)-1H-pyridin-2-one;

5-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-oxo-1,6-dihydropyridine-2-carbaldehyde;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-{[5-(hydroxymethyl)pyrazin-2-yl]methyl}-6-methylpyridin-2(1H)-one;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzamide;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[3-(piperazin-1-ylcarbonyl)phenyl]pyridin-2(1H)-one hydrochloride;

3-bromo-4-[(2,4-difluorobenzyl)amino]-1-(3-fluorobenzyl)pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[5-methylpyrazin-2-yl]methyl]pyridin-2(1H)-one;

3-chloro-4-[(2,4-difluorobenzyl)oxy]-1-[5-(hydroxymethyl)-2-methylphenyl]-6-methylpyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

3-Bromo-1-(3-fluoro-benzyl)-4-(4-fluoro-benzyloxy)-1H-pyridin-2-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[3-

(morpholin-4-ylcarbonyl)phenyl]pyridin-2(1H)-one;
3-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-
benzoic acid methyl ester;
3-bromo-1-(3-fluorobenzyl)-4-{[2-(
(hydroxymethyl)benzyl]oxy}pyridin-2(1H)-one;
3-Bromo-1-(3-fluoro-benzyl)-4-(2-hydroxymethyl-
benzyloxy)-1H-pyridin-2-one;
1-Benzo[1,3]dioxol-5-ylmethyl-3-bromo-4-(2,4-difluoro-
benzyloxy)-1H-pyridin-2-one;
3-bromo-4-[(2,6-difluorobenzyl)oxy]-6-methyl-1-(pyridin-
4-ylmethyl)pyridin-2(1H)-one;
3-bromo-4-[(3-chlorobenzyl)oxy]-1-(3-
fluorobenzyl)pyridin-2(1H)-one;
3-bromo-4-[(3-chlorobenzyl)oxy]-1-(3-
fluorobenzyl)pyridin-2(1H)-one;
3-Bromo-4-(3-chloro-benzyloxy)-1-(3-fluoro-benzyl)-1H-
pyridin-2-one;
4-(benzyloxy)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-
one;
4-Benzyloxy-3-bromo-1-(3-fluoro-benzyl)-1H-pyridin-2-one;
3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-[3-(
piperidine-1-carbonyl)-benzyl]-1H-pyridin-2-one;
3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-
oxopyridin-1(2H)-yl]-N,N-dimethylbenzamide;
3-[3-Chloro-4-(2,4-difluoro-benzyloxy)-2-oxo-2H-pyridin-
1-ylmethyl]-2-fluoro-benzoic acid methyl ester;
1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]-3-iodopyridin-
2(1H)-one;
1-(3-Fluoro-benzyl)-4-(4-fluoro-benzyloxy)-3-iodo-1H-
pyridin-2-one;
N-(3-aminopropyl)-4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-
6-methyl-2-oxopyridin-1(2H)-yl]benzamide hydrochloride;

4-{[3-bromo-4-[(4-fluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;

4-[3-Bromo-4-(4-fluoro-benzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzonitrile;

3-Bromo-1-(3-fluoro-benzyl)-4-(2,3,4-trifluoro-benzyloxy)-1H-pyridin-2-one;

1-benzyl-4-(benzyloxy)-3-bromopyridin-2(1H)-one;

5-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}-N-(2-hydroxyethyl)-N-methylpyrazine-2-carboxamide;

4-(4-Benzyloxy-3-bromo-2-oxo-2H-pyridin-1-ylmethyl)-benzonitrile;

3-bromo-1-(2,4-difluorobenzyl)-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;

3-Bromo-1-(2,4-difluoro-benzyl)-4-(2,4-difluoro-benzyloxy)-1H-pyridin-2-one;

4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-(2-hydroxyethyl)benzamide;

3-bromo-4-[(4-fluorobenzyl)oxy]-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;

1-Benzyl-4-benzyloxy-3-bromo-1H-pyridin-2-one;

3-bromo-1-(cyclopropylmethyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-(4-Aminomethyl-benzyl)-4-benzyloxy-3-bromo-1H-pyridin-2-one;

3-bromo-1-(4-fluorobenzyl)-4-[(4-fluorobenzyl)amino]-6-methylpyridin-2(1H)-one;

3-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzoic acid methyl ester;

5-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}-N,N-dimethylpyrazine-2-carboxamide;

3-bromo-4-[(4-fluorobenzyl)oxy]-6-methyl-1-(pyridin-2-ylmethyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-dimethylphenyl)-6-methylpyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-1-(4-bromobenzyl)pyridin-2(1H)-one;

3-bromo-4-hydroxy-1-(4-hydroxybenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-[2-(trifluoromethyl)benzyl]pyridin-2(1H)-one;

1-benzyl-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-(piperidin-3-ylmethyl)pyridin-2(1H)-one hydrochloride;

1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-4-ylmethyl(phenyl)carbamate;

4-(benzylamino)-1-(3-fluorobenzyl)-6-methyl-3-nitropyridin-2(1H)-one;

tert-butyl 4-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]piperazine-1-carboxylate;

ethyl [4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]acetate;

N-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]benzenesulfonamide;

3-bromo-4-[(4-tert-butylbenzyl)oxy]-1-(3-fluorobenzyl)pyridin-2(1H)-one;

N-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]-1-phenylmethanesulfonamide;

1-(biphenyl-2-ylmethyl)-3-bromo-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

4-(biphenyl-2-ylmethoxy)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorophenyl)amino]-1-(3-fluorobenzyl)pyridin-2(1H)-one;
4-anilino-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one;
methyl 4-{[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]amino}benzoate;
3-bromo-1-(3-fluorobenzyl)-4-[(3,4,5-trimethoxyphenyl)amino]pyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-[4-(4-fluorophenyl)piperazin-1-yl]pyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-(4-methylpiperazin-1-yl)pyridin-2(1H)-one trifluoroacetate;
N-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]-2,5-difluorobenzamide;
N-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]-2,4-difluorobenzamide;
3-bromo-1-(cyclohexylmethyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;
3-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]propanoic acid;
N-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]-N'-(2,4-difluorophenyl)urea;
3-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]propanamide;
4-(benzyloxy)-3-bromo-1-(3-morpholin-4-yl-3-oxopropyl)pyridin-2(1H)-one;
N-(3-aminopropyl)-3-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]propanamide hydrochloride;
4-(benzyloxy)-3-bromo-1-(3-oxo-3-piperazin-1-ylpropyl)pyridin-2(1H)-one hydrochloride;
4-(benzyloxy)-3-bromo-1-(2-morpholin-4-ylethyl)pyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-{[4-fluoro-2-

(trifluoromethyl)benzyl]amino}pyridin-2(1H)-one;
N-(2-aminoethyl)-3-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]propanamide hydrochloride;
[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]acetic acid;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(tetrahydrofuran-2-ylmethyl)pyridin-2(1H)-one;
4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(tetrahydrofuran-2-ylmethyl)pyridin-2(1H)-one;
methyl 3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridine-1(2H)-carboxylate;
1-allyl-3-(2,4-difluorobenzyl)-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;
4-(benzyloxy)-1-(2,2-diethoxyethyl)pyridin-2(1H)-one;
methyl N-acetyl-3-[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]alaninate;
benzyl N-acetyl-3-[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]alaninate;
benzyl N-[(benzyloxy)carbonyl]-3-[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]alaninate;
4-(benzyloxy)-1-(2-oxopropyl)pyridin-2(1H)-one;
5-{[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]methyl}-5-methylimidazolidine-2,4-dione;
ethyl [4-(benzyloxy)-2-oxopyridin-1(2H)-yl]acetate;
2-[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]acetamide;
1-benzyl-4-(benzyloxy)-3,5-dibromopyridin-2(1H)-one;
4-(benzyloxy)-1-ethylpyridin-2(1H)-one;
4-(benzyloxy)-1-(4-tert-butylbenzyl)pyridin-2(1H)-one;
4-{[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;
tert-butyl 3-{[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]methyl}piperidine-1-carboxylate;

1,3-dibenzyl-4-hydroxy-6-methylpyridin-2 (1H) -one;
1-benzyl-6-methyl-2-oxo-1,2-dihydropyridin-4-yl
methanesulfonate;
4-(benzyloxy)-1-(4-bromobenzyl)pyridin-2 (1H) -one;
4-(benzyloxy)-3-bromopyridin-2 (1H) -one;
4-(benzyloxy)-3-bromo-1-[2-(trifluoromethyl)benzyl]pyridin-2 (1H) -one;
1-benzyl-4-(1-naphthylmethoxy)pyridin-2 (1H) -one;
1-benzyl-4-(benzylthio)-3,5-dibromopyridin-2 (1H) -one;
1-benzyl-4-[(2,6-dichlorobenzyl)oxy]pyridin-2 (1H) -one;
1-benzyl-3-[(benzylamino)methyl]-4-(benzyloxy)pyridin-
2 (1H) -one;
1-benzyl-4-(benzyloxy)-3-{[(2-cyclohexylethyl)amino]methyl}pyridin-2 (1H) -one;
1-benzyl-4-(benzylthio)-5-methylpyridin-2 (1H) -one;
1-benzyl-3-bromo-6-methyl-2-oxo-1,2-dihydropyridin-4-yl
methanesulfonate;
1-benzyl-3-bromo-6-methyl-4-{[2-(trifluoromethyl)benzyl]oxy}pyridin-2 (1H) -one;
1-benzyl-6-methyl-2-oxo-1,2-dihydropyridin-4-yl 4-
bromobenzenesulfonate;
1-benzyl-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2 (1H) -
one;
1-benzyl-3-bromo-6-methyl-2-oxo-1,2-dihydropyridin-4-yl
4-bromobenzenesulfonate;
4-phenoxy-1-{[2-(trimethylsilyl)ethoxy]methyl}pyridin-
2 (1H) -one;
1-benzyl-4-phenoxy-2 (1H) -one;
1-(4-methoxybenzyl)-4-phenoxy-2 (1H) -one;
3-bromo-4-hydroxy-1-(4-hydroxybenzyl)pyridin-2 (1H) -one
hydrochloride;
4-(benzyloxy)-3-bromo-1-(piperidin-3-ylmethyl)pyridin-

2 (1H) -one;
 1-benzyl-4-[(2,6-dichlorobenzyl)oxy]pyridin-2 (1H) -one;
 1-benzyl-4-(benzyloxy)-3,5-dibromopyridin-2 (1H) -one;
 3-bromo-1-(3-fluorobenzyl)-4-[(E)-2-(4-fluorophenyl)vinyl]pyridin-2 (1H) -one;
 1-benzyl-4-(benzyloxy)-2-oxo-1,2-dihydropyridine-3-carbaldehyde;
 1-benzyl-4-(benzyloxy)pyridin-2 (1H) -one;
 1-benzyl-4-(benzyloxy)pyridin-2 (1H) -one;
 1-benzyl-4-(benzylthio)pyridin-2 (1H) -one;
 methyl 4-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1 (2H) -yl]benzoate;
 benzyl (5-nitro-2,6-dioxo-3,6-dihydropyrimidin-1 (2H) -yl) acetate;
 ethyl 3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxo-2H-1,2'-bipyridine-5'-carboxylate;
 4-(benzyloxy)-1-(4-methylbenzyl)pyridin-2 (1H) -one;
 [5-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-2-methyl-6-oxo-1,6-dihydropyridin-3-yl]methyl carbamate;
 4-(benzyloxy)-1-(4-chlorobenzyl)pyridin-2 (1H) -one;
 methyl (2E)-4-[4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1 (2H) -yl]but-2-enoate;
 4-(benzyloxy)-1-(2-fluorobenzyl)pyridin-2 (1H) -one;
 tert-butyl 4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1 (2H) -yl]methyl}piperidine-1-carboxylate;
 4-(benzyloxy)-1-(3-fluorobenzyl)pyridin-2 (1H) -one;
 3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-5-(1,2-dihydroxyethyl)-6-methylpyridin-2 (1H) -one;
 1-benzyl-4-hydroxy-6-methylpyridin-2 (1H) -one;
 4-([3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-

4-yl]oxy)methyl)benzonitrile;

1-benzyl-4-(benzyloxy)-6-methylpyridin-2(1H)-one;

5-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-2-methyl-6-oxo-1,6-dihydropyridine-3-carbaldehyde oxime;

1-benzyl-4-(benzylthio)-3-methylpyridin-2(1H)-one;

1-benzyl-4-[(4-methylbenzyl)oxy]pyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3,5-dibromo-6-methylpyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-3,5-dibromo-6-methylpyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-(1-phenylethoxy)pyridin-2(1H)-one;

4-(benzyloxy)-1-[4-(trifluoromethyl)benzyl]pyridin-2(1H)-one;

2-([3-bromo-2-oxo-1-(pyridin-3-ylmethyl)-1,2-dihydropyridin-4-yl]oxy)methyl)-5-fluorobenzonitrile;

5-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-2-methyl-6-oxo-1,6-dihydropyridine-3-carbonitrile;

4-(benzyloxy)-1-(3-fluorobenzyl)-3-(trifluoromethyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-methyl-5-oxiran-2-ylpyridin-2(1H)-one;

1-benzyl-4-[(3-chlorobenzyl)oxy]pyridin-2(1H)-one;

1-benzyl-4-[(3-chlorobenzyl)oxy]pyridin-2(1H)-one;

5-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-2-methyl-6-oxo-1,6-dihydropyridine-3-carbaldehyde;

tert-butyl 3-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}piperidine-1-carboxylate;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-

difluorophenyl)-6-methyl-5-vinylpyridin-2(1H)-one;
4-(benzyloxy)-1-[4-(trifluoromethoxy)benzyl]pyridin-2(1H)-one;
3-bromo-4-[(4-chlorobenzyl)oxy]-1-[2-(phenylthio)ethyl]pyridin-2(1H)-one;
3-Bromo-4-(4-chloro-benzyloxy)-1-(2-phenylsulfanyl-ethyl)-1H-pyridin-2-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-(2-morpholin-4-ylethyl)pyridin-2(1H)-one;
4-[(2,4-difluorobenzyl)oxy]-6-(hydroxymethyl)-1-(pyridin-3-ylmethyl)pyridin-2(1H)-one;
4-{[2-(Aminomethyl)-4-fluorobenzyl]oxy}-3-bromo-1-(2,6-difluorophenyl)-6-methylpyridin-2(1H)-one trifluoroacetate;
4-(benzyloxy)-1-(4-fluorobenzyl)pyridin-2(1H)-one;
4-(benzyloxy)-1-(4-fluorobenzyl)pyridin-2(1H)-one;
4-Benzyloxy-3-bromo-1-methanesulfonyl-1H-pyridin-2-one;
tert-butyl 4-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]piperidine-1-carboxylate;
1-benzyl-4-(benzyloxy)-3-vinylpyridin-2(1H)-one;
4-(benzyloxy)-1-[4-(methylthio)benzyl]pyridin-2(1H)-one;
3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(2-methyl-4-methylamino-pyrimidin-5-ylmethyl)-1H-pyridin-2-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;
1-benzyl-3-bromo-4-{[2-(trifluoromethyl)benzyl]oxy}pyridin-2(1H)-one;
1-benzyl-3-bromo-4-{[2-(trifluoromethyl)benzyl]oxy}pyridin-2(1H)-one;
4-[(2,4-difluorobenzyl)oxy]-1-[5-(hydroxymethyl)-2-methylphenyl]-6-methylpyridin-2(1H)-one;
4-(benzyloxy)-1-[4-(methylsulfonyl)benzyl]pyridin-2(1H)-one;

4-Phenoxy-1H-pyridin-2-one;
1-benzyl-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one;
1-benzyl-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one;
methyl 4-{[4-(benzyloxy)-2-oxopyridin-1(2H)-yl]methyl}benzoate;
4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-methylpyridin-2(1H)-one;
1-(3-fluorobenzyl)-4-(phenylethynyl)pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-(piperidin-4-ylmethyl)pyridin-2(1H)-one hydrochloride;
4-(benzyloxy)-3-bromo-1-(piperidin-4-ylmethyl)pyridin-2(1H)-one hydrochloride;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[2-(methylthio)pyrimidin-4-yl]pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-piperidin-4-ylpyridin-2(1H)-one hydrochloride;
4-Benzyloxy-1-difluoromethyl-1H-pyridin-2-one;
4-Benzyloxy-3-bromo-1-(2-chloro-phenyl)-6-methyl-1H-pyridin-2-one;
3-Bromo-6-methyl-1-pyridin-3-ylmethyl-4-[(pyridin-3-ylmethyl)-amino]-1H-pyridin-2-one;
1-(3,4-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (2,4-difluoro-phenyl)-amide;
1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (2,4-difluoro-phenyl)-amide;
5-Chloro-1-(2,6-dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (2,4-difluoro-phenyl)-amide;
5-Chloro-1-(2,6-dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid methyl-phenyl-amide;
1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid benzylamide;
1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-

carboxylic acid (3-dimethylamino-propyl)-amide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (2-morpholin-4-yl-ethyl)-amide;

N-[5-Acetyl-1-(4-chloro-benzyl)-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl]-4-chloro-benzamide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid N'-(3-chloro-5-trifluoromethyl-pyridin-2-yl)-hydrazide;

N-allyl-2-[(1-benzyl-6-oxo-1,6-dihydropyridin-3-yl)carbonyl]hydrazinecarbothioamide;

1-Benzyl-5-[5-(3,4-dichloro-benzylsulfanyl)-[1,3,4]oxadiazol-2-yl]-1H-pyridin-2-one;

N'-{[(1-benzyl-6-oxo-1,6-dihydropyridin-3-yl)carbonyl]oxy}pyridine-4-carboximidamide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid 3-trifluoromethyl-benzylamide;

1-Benzyl-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (2-morpholin-4-yl-ethyl)-amide;

5-[4-(3-Chloro-phenyl)-piperazine-1-carbonyl]-1-(3,4-dichloro-benzyl)-1H-pyridin-2-one;

5-Chloro-1-(2,6-dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid benzylamide;

1-(4-Chloro-benzyl)-5-[3-(4-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1H-pyridin-2-one;

1-(4-Chloro-benzyl)-5-[3-(4-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1H-pyridin-2-one;

2-Chloro-N-[1-(2,6-dichloro-benzyl)-6-oxo-5-trifluoromethyl-1,6-dihydro-pyridin-3-yl]-4-fluoro-benzamide;

N-[1-(2,6-Dichloro-benzyl)-6-oxo-5-trifluoromethyl-1,6-dihydro-pyridin-3-yl]-4-isopropoxy-benzamide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (4-trifluoromethoxy-phenyl)-amide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (3-trifluoromethyl-phenyl)-amide;

5-Chloro-1-(2,6-dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (3-trifluoromethyl-phenyl)-amide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (4-chloro-phenyl)-amide;

1-(2,6-Dichloro-benzyl)-6-oxo-1,6-dihydro-pyridine-3-carboxylic acid (2-dimethylamino-ethyl)-amide;

5-Methyl-1-phenyl-1H-pyridin-2-one;

3-Bromo-1-(3-fluoro-benzyl)-4-(3-methoxy-phenyl)-1H-pyridin-2-one;

3-Bromo-1-(3-fluoro-benzyl)-4-(3-isopropyl-phenyl)-1H-pyridin-2-one;

3'-Bromo-1'-(3-fluoro-benzyl)-6-methoxy-1'H-[3,4']bipyridinyl-2'-one;

4-Benzo[1,3]dioxol-5-yl-3-bromo-1-(3-fluoro-benzyl)-1H-pyridin-2-one;

3-Bromo-1-(3-fluoro-benzyl)-4-thiophen-3-yl-1H-pyridin-2-one;

3-Bromo-1-(3-fluoro-benzyl)-4-(3-trifluoromethyl-phenyl)-1H-pyridin-2-one;

3-Bromo-1-(3-fluoro-benzyl)-4-naphthalen-2-yl-1H-pyridin-2-one;

3-Bromo-1-(3-fluoro-benzyl)-4-(4-fluoro-phenyl)-1H-pyridin-2-one;

1-Benzenesulfonyl-4-benzyloxy-3-bromo-1H-pyridin-2-one;

4-[3-Amino-1-(2,4-difluoro-phenyl)-propoxy]-3-bromo-6-methyl-1-pyridin-3-ylmethyl-1H-pyridin-2-one;

1-(4-Bromo-2,6-difluoro-phenyl)-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;

2-[1-(4-Amino-2-methyl-pyrimidin-5-ylmethyl)-3-bromo-6-methyl-2-oxo-1,2-dihydro-pyridin-4-ylloxymethyl]-5-fluoro-

benzonitrile;

4-(2,4-Difluoro-benzyloxy)-6-methyl-1-(2,4,6-trifluorophenyl)-1H-pyridin-2-one;

1-(2-Chloro-4-hydroxy-phenyl)-4-(2,4-difluoro-benzyloxy)-6-methyl-1H-pyridin-2-one;

3-[4-(2,4-Difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-benzoic acid methyl ester;

3-Bromo-1-(2,6-difluoro-phenyl)-4-methoxy-6-methyl-5-vinyl-1H-pyridin-2-one;

3-Bromo-1-(2,6-difluoro-phenyl)-4-methoxy-6-methyl-5-styryl-1H-pyridin-2-one;

1-(2,6-Difluoro-phenyl)-4-methoxy-6-methyl-5-phenethyl-1H-pyridin-2-one;

3-Bromo-1-(2,6-difluoro-phenyl)-4-methoxy-6-methyl-5-phenethyl-1H-pyridin-2-one;

1-(1H-indazol-5-yl)-4-(1H-indazol-5-ylamino)-6-methylpyridin-2(1H)-one;

5-Bromo-4-(2,4-difluoro-benzyloxy)-1-(2,6-difluorophenyl)-2-[2-(2,4-difluoro-phenyl)-ethyl]-6-oxo-1,6-dihydropyridine-3-carbaldehyde;

4-[3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-pyrimidine-2-carbonitrile;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-[1,2']bipyridinyl-5'-carboxylic acid;

3-Bromo-4-(5-carboxy-pyridin-2-yloxy)-6-methyl-2-oxo-2H-[1,2']bipyridinyl-5'-carboxylic acid;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6,6'-dimethyl-2-oxo-2H-[1,2']bipyridinyl-3'-carbonitrile;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-[1,2']bipyridinyl-5'-carboxylic acid methylamide;

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-hydroxy-ethyl)-amide;

3-Bromo-4- (2,4-difluoro-benzyloxy) -6-methyl-2-oxo-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-methoxy-ethyl)-amide;

3-Bromo-1- (2,6-difluoro-phenyl) -4-methoxy-6-methyl-5- (4-methyl-benzyl) -1H-pyridin-2-one;

3-bromo-4- [(2,4-difluorobenzyl) oxy] -1- (2,6-difluorophenyl) -5- (1,2-dihydroxy-2-phenylethyl) -6-methylpyridin-2 (1H) -one;

3-bromo-4- [(2,4-difluorobenzyl) oxy] -5' - (1-hydroxy-1-methylethyl) -6-methyl-2H-1,2' -bipyridin-2-one;

4-Benzyloxy-1H-pyridin-2-one;

4-Benzyloxy-3-methyl-1H-pyridin-2-one;

2-Oxo-6-phenethyl-1,2-dihydro-pyridine-3-carbonitrile;

2-Oxo-6-phenyl-1,2-dihydro-pyridine-3-carbonitrile;

6-Oxo-1,6-dihydro- [2,3']bipyridinyl-5-carbonitrile;

6-Oxo-1,6-dihydro- [2,3']bipyridinyl-5-carboxylic acid;

3- { [4- (benzyloxy) -3-bromo-2-oxopyridin-1 (2H) -yl]methyl}benzamide;

3-bromo-4- [(4-fluorobenzyl) oxy] -1- (4-methoxybenzyl) pyridin-2 (1H) -one;

3-bromo-4- [(4-fluorobenzyl) oxy] -1- (4-methoxybenzyl) pyridin-2 (1H) -one;

3-bromo-4- [(2,4-difluorobenzyl) oxy] -1- [2-fluoro-5- (hydroxymethyl) phenyl] -6-methylpyridin-2 (1H) -one;

3-chloro-1- (4-fluorobenzyl) -4- [(4-fluorobenzyl) oxy] pyridin-2 (1H) -one;

3-chloro-1- (4-fluorobenzyl) -4- [(4-fluorobenzyl) oxy] pyridin-2 (1H) -one;

3-bromo-1- (3-chlorobenzyl) -4- [(4-fluorobenzyl) oxy] pyridin-2 (1H) -one;

3-bromo-4- [(3,4-difluorobenzyl) oxy] -1- (3-fluorobenzyl) pyridin-2 (1H) -one;

3- [3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-

oxypyridin-1(2H)-yl]-4-methylbenzoic acid;
3-bromo-1-(3-chlorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;
3-bromo-1-(3-chlorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;
4-{[3-chloro-4-[(2,4-difluorobenzyl)amino]-6-methyl-2-oxypyridin-1(2H)-yl]methyl}benzonitrile trifluoroacetate;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{[5-(1-hydroxy-1-methylethyl)pyrazin-2-yl]methyl}-6-methylpyridin-2(1H)-one;
4-(benzylamino)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one;
4-(benzylamino)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one;
2-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxypyridin-1(2H)-yl]methyl}benzonitrile;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[2-fluoro-6-(4-methylpiperazin-1-yl)phenyl]-6-methylpyridin-2(1H)-one trifluoroacetate;
4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxypyridin-1(2H)-yl]-N-methylbenzamide;
1-[2-(aminomethyl)benzyl]-3-bromo-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;
3-bromo-1-(4-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;
1-[2-(aminomethyl)benzyl]-3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[3-(piperidin-1-ylcarbonyl)phenyl]pyridin-2(1H)-one;
1-benzyl-3-bromo-4-[(4-chlorobenzyl)oxy]pyridin-2(1H)-one;
4-[(2,4-difluorobenzyl)oxy]-1-(3-fluorobenzyl)-3-methylpyridin-2(1H)-one;

4-(benzyloxy)-1-[4-(benzyloxy)benzyl]-3-bromopyridin-2(1H)-one;

4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-hydroxybenzamide;

4-(benzyloxy)-3-bromo-1-[4-(trifluoromethyl)benzyl]pyridin-2(1H)-one;

3-bromo-1-(cyclopropylmethyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(cyclopropylmethyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

2-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-({5-[(methylamino)methyl]pyrazin-2-yl}methyl)pyridin-2(1H)-one trifluoroacetate;

3-bromo-1-(3-fluorobenzyl)-4-[(2-methylbenzyl)oxy]pyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-[(2-methylbenzyl)oxy]pyridin-2(1H)-one;

methyl 3-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}benzoate;

3-bromo-1-(3-fluorobenzyl)-6-methyl-4-(2-phenylethyl)pyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-6-methyl-4-(2-phenylethyl)pyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(4-methylbenzyl)oxy]pyridin-2(1H)-

one;

4-(benzyloxy)-1-(3-fluorobenzyl)-3-iodopyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[3-

(hydroxymethyl)phenyl]-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-1-(3-fluorobenzyl)-3-iodopyridin-2(1H)-one;
3-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-

oxopyridin-1(2H)-yl]methyl}benzoic acid;

3-bromo-4-[(4-fluorobenzyl)oxy]-1-[2-

(hydroxymethyl)benzyl]pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-[(5-{[(2-hydroxyethyl)(methyl)amino]methyl}pyrazin-2-yl)methyl]-6-methylpyridin-2(1H)-one trifluoroacetate (salt);

4-(benzyloxy)-3-bromo-1-[(6-fluoropyridin-3-yl)methyl]pyridin-2(1H)-one;

3-bromo-4-[(4-chlorobenzyl)oxy]-1-(4-fluorobenzyl)pyridin-2(1H)-one;

3-bromo-4-[(4-chloro-2-fluorobenzyl)amino]-1-(3-fluorobenzyl)pyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-ethylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-ethylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-ethylpyridin-2(1H)-one;

2-(2-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}phenyl)acetamide;

1-benzyl-3-bromo-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one;

1-benzyl-3-bromo-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one;

methyl 2-{[3-bromo-4-[(4-fluorobenzyl)oxy]-2-oxopyridin-1(2H)-yl]methyl}benzoate;

3-bromo-1-(2,6-dichlorophenyl)-4-[2-(4-fluorophenyl)ethyl]-6-methylpyridin-2(1H)-one;

3-bromo-1-(2,6-dichlorophenyl)-4-[2-(4-

fluorophenyl) ethyl] -6-methylpyridin-2 (1H) -one;
3-bromo-4- [(2,4-difluorobenzyl) oxy] -1- {5-
[(isopropylamino) methyl] -2-methylphenyl} -6-methylpyridin-
2 (1H) -one hydrochloride;
3-bromo-1- (3-fluorobenzyl) -4- (2-phenylethyl) pyridin-
2 (1H) -one;
N- {3- [3-bromo-4- [(2,4-difluorobenzyl) oxy] -6-methyl-2-
oxopyridin-1 (2H) -yl] benzyl} -N' -methylurea;
3-chloro-4- [(2,4-difluorobenzyl) oxy] -1- [3-
(hydroxymethyl) phenyl] -6-methylpyridin-2 (1H) -one;
3-bromo-1- (3-fluorobenzyl) -4- [(3-
fluorobenzyl) oxy] pyridin-2 (1H) -one;
4- (benzyloxy) -3-bromo-1- [2- (2-thienyl) ethyl] pyridin-
2 (1H) -one;
4- (benzyloxy) -3-bromo-1- [2- (2-thienyl) ethyl] pyridin-
2 (1H) -one;
3-bromo-4- [(2,4-difluorobenzyl) amino] -1- (2,6-
difluorophenyl) -6-methylpyridin-2 (1H) -one trifluoroacetate;
3-bromo-4- [(2,4-difluorobenzyl) amino] -1- (2,6-
difluorophenyl) -6-methylpyridin-2 (1H) -one trifluoroacetate;
3-bromo-4- [(4-chlorobenzyl) oxy] -1- (4-
methoxybenzyl) pyridin-2 (1H) -one;
3-bromo-4- [(4-chlorobenzyl) oxy] -1- (4-
methoxybenzyl) pyridin-2 (1H) -one;
3-bromo-1- (4-chlorobenzyl) -4- [(4-
chlorobenzyl) oxy] pyridin-2 (1H) -one;
3-bromo-1- (3-fluorobenzyl) -4- [(4-
methoxybenzyl) oxy] pyridin-2 (1H) -one;
3-bromo-1- (3,5-dibromo-2,6-difluoro-4-hydroxyphenyl) -4-
[(2,4-difluorobenzyl) oxy] -6-methylpyridin-2 (1H) -one;
4- (benzyloxy) -3-bromo-1- [4-
(trifluoromethoxy) benzyl] pyridin-2 (1H) -one;

4-(benzyloxy)-3-bromo-1-[4-(trifluoromethoxy)benzyl]pyridin-2(1H)-one;
N'-{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}-N,N-dimethylurea;
3-bromo-4-[(4-fluorobenzyl)oxy]-1-[4-(trifluoromethyl)benzyl]pyridin-2(1H)-one;
2-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}benzamide;
N-{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}morpholine-4-carboxamide;
N-{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}methanesulfonamide;
4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N-isopropylbenzamide;
4-(allylamino)-3-bromo-1-(2,6-difluorophenyl)-5-iodo-6-methylpyridin-2(1H)-one;
4-(allylamino)-3-bromo-1-(2,6-difluorophenyl)-5-iodo-6-methylpyridin-2(1H)-one;
(4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}phenyl)acetic acid;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[4-(pyrrolidin-1-ylcarbonyl)phenyl]pyridin-2(1H)-one;
1-benzyl-4-(benzyloxy)-3-iodopyridin-2(1H)-one;
1-(biphenyl-4-ylmethyl)-3-bromo-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;
4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoic acid;
4-(benzyloxy)-3-bromo-1-[2-(3-thienyl)ethyl]pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-[2-(3-thienyl)ethyl]pyridin-2(1H)-one;
3-bromo-4-[(4-fluorobenzyl)oxy]-1-[3-

(trifluoromethyl)benzyl]pyridin-2(1H)-one;
N-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]-4-fluorobenzamide;
methyl 3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzylcarbamate;
1-benzyl-4-(benzylthio)-3-bromopyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-(4-tert-butylbenzyl)pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-(4-tert-butylbenzyl)pyridin-2(1H)-one;
N-{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}-2-methoxyacetamide;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-({5-[(dimethylamino)methyl]pyrazin-2-yl)methyl}-6-methylpyridin-2(1H)-one trifluoroacetate;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[4-(piperazin-1-ylcarbonyl)phenyl]pyridin-2(1H)-one hydrochloride;
4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N,N-bis(2-hydroxyethyl)benzamide;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{5-[(dimethylamino)methyl]-2-methylphenyl}-6-methylpyridin-2(1H)-one hydrochloride;
1-benzyl-3-bromo-4-(2-phenylethyl)pyridin-2(1H)-one;
1-(3-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]-3-methylpyridin-2(1H)-one;
4-(benzyloxy)-1-(piperidin-3-ylmethyl)pyridin-2(1H)-one trifluoroacetate;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[4-(morpholin-4-ylcarbonyl)phenyl]pyridin-2(1H)-one;
4-(benzyloxy)-1-(3-fluorobenzyl)-3-methylpyridin-2(1H)-one;

N^1 -{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}glycinamide hydrochloride;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-5-iodo-6-methylpyridin-2(1H)-one;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-[4-(piperidin-1-ylcarbonyl)phenyl]pyridin-2(1H)-one;
 N -[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridin-4-yl]-2,6-difluorobenzamide;
2-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzonitrile;
5-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}- N -methylpyrazine-2-carboxamide;
3-chloro-4-[(2,4-difluorobenzyl)amino]-1-(2,6-difluorophenyl)-6-methylpyridin-2(1H)-one;
3-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzoic acid;
3-bromo-1-(3-fluorobenzyl)-4-[(3-fluorobenzyl)amino]pyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-[(3-methoxybenzyl)oxy]pyridin-2(1H)-one;
3-bromo-1-(4-*tert*-butylbenzyl)-4-[(2,4-difluorobenzyl)oxy]pyridin-2(1H)-one;
 N -{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}acetamide;
2-({3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}amino)-2-oxoethyl acetate;
1-benzyl-4-(benzyloxy)-3-methylpyridin-2(1H)-one;
 N -{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}urea;
1-benzyl-4-(benzyloxy)-3-ethylpyridin-2(1H)-one;
 N -{3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]benzyl}-2-hydroxyacetamide;

3-bromo-4-[(4-chlorobenzyl)oxy]-1-(2-phenylethyl)pyridin-2(1H)-one;

3-bromo-1-(3-chlorobenzyl)-4-[(4-chlorobenzyl)oxy]pyridin-2(1H)-one;

1-[3-(aminomethyl)phenyl]-3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methylpyridin-2(1H)-one;

2-{[4-(benzyloxy)-3-bromo-2-oxypyridin-1(2H)-yl]methyl}benzamide;

1-(4-fluorobenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

1-[2-(aminomethyl)benzyl]-4-(benzyloxy)-3-bromopyridin-2(1H)-one;

methyl 3-[4-(benzyloxy)-3-bromo-2-oxypyridin-1(2H)-yl]propanoate;

1-benzyl-4-(benzyloxy)-3-methylpyridin-2(1H)-one;

4-(allylamino)-1-(2,6-difluorophenyl)-5-iodo-6-methylpyridin-2(1H)-one;

4-(allylamino)-1-(2,6-difluorophenyl)-5-iodo-6-methylpyridin-2(1H)-one;

3-bromo-1-(3-fluorobenzyl)-4-(phenylethynyl)pyridin-2(1H)-one;

4-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxypyridin-1(2H)-yl]-N,N-dimethylbenzamide;

{4-[(4-(benzyloxy)-3-bromo-1-[4-(carboxymethyl)benzyl]-1,2-dihydropyridin-2-yl]oxy)methyl}phenyl}acetic acid;

4-(benzyloxy)-3-bromo-1-[3-(trifluoromethyl)benzyl]pyridin-2(1H)-one;

4-(benzyloxy)-3-ethynyl-1-(3-fluorobenzyl)pyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-{3-[(dimethylamino)methyl]phenyl}-6-methylpyridin-2(1H)-one;

4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one;

1-benzyl-3-bromo-4-(phenylethynyl)pyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-{[4-(trifluoromethyl)benzyl]oxy}pyridin-2(1H)-one;
4-(benzylamino)-3-bromo-1-(2,6-difluorophenyl)-5-iodo-6-methylpyridin-2(1H)-one;
4-[(2,4-difluorobenzyl)oxy]-1-(4-methoxybenzyl)-6-methylpyridin-2(1H)-one;
4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one hydrobromide;
4-(benzyloxy)-3-bromo-1-[4-(morpholin-4-ylcarbonyl)phenyl]pyridin-2(1H)-one;
5-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-oxo-1,6-dihydropyridine-2-carboxylic acid;
1-benzyl-3-bromo-4-[(2,6-dichlorobenzyl)oxy]pyridin-2(1H)-one;
3-[3-chloro-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-2-methylbenzoic acid;
4-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]benzoic acid;
ethyl N-(5-{[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]methyl}-2-methylpyrimidin-4-yl)glycinate trifluoroacetate;
3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-6-methyl-5-[(E)-2-phenylvinyl]pyridin-2(1H)-one;
3-bromo-1-(3-fluorobenzyl)-4-{[3-(trifluoromethyl)benzyl]amino}pyridin-2(1H)-one;
3-bromo-4-[(4-fluorobenzyl)oxy]-1-(3-phenylpropyl)pyridin-2(1H)-one;
3-bromo-1-(4-tert-butylbenzyl)-4-[(4-fluorobenzyl)oxy]pyridin-2(1H)-one;

4-(allylamino)-3-bromo-1-(2,6-difluorophenyl)-6-methylpyridin-2(1H)-one;

1-cyclohexyl-4-[(2,4-difluorobenzyl)oxy]-3,6-dimethylpyridin-2(1H)-one;

3-bromo-4-[(2,4-difluorobenzyl)oxy]-1-(2,6-difluorophenyl)-5-(hydroxymethyl)-6-methylpyridin-2(1H)-one;

1-benzyl-4-(benzyloxy)-2-oxo-1,2-dihydropyridine-3-carbaldehyde;

4-[(2,4-difluorobenzyl)oxy]-6-methyl-1-prop-2-yn-1-ylpyridin-2(1H)-one;

ethyl 3-[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]propanoate;

1-benzyl-4-(benzyloxy)-3-(hydroxymethyl)pyridin-2(1H)-one;

or a pharmaceutically acceptable salt thereof.

3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(5-methylpyrazin-2-ylmethyl)-1H-pyridin-2-one

3-Chloro-4-(2,4-difluoro-benzyloxy)-1-(5-hydroxymethylpyrazin-2-ylmethyl)-6-methyl-1H-pyridin-2-one

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-(2,3-dihydro-1H-indol-5-ylmethyl)-1H-pyridin-2-one

3-Bromo-4-(2,4-difluoro-benzyloxy)-1-[1-(2-hydroxyacetyl)-2,3-dihydro-1H-indol-5-ylmethyl]-6-methyl-1H-pyridin-2-one

3-Bromo-4-(2,4-difluoro-benzyloxy)-6-methyl-1-(1H-pyrazol-3-ylmethyl)-1H-pyridin-2-one

3-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-4,N-dimethyl-benzamide

3-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-4-methyl-benzamide

3-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-4-fluoro-N-methyl-benzamide

4-Chloro-3-[3-chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-N-methyl-benzamide

3-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-4-fluoro-benzamide

4-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-yl]-3,N-dimethyl-benzamide

3-Chloro-4-(2,4-difluoro-benzyloxy)-1-[4-(1,2-dihydroxy-ethyl)-2-methyl-phenyl]-6-methyl-1H-pyridin-2-one

N-{4-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-phenyl}-2-hydroxy-acetamide

1-Hydroxy-cyclopropanecarboxylic acid 4-[3-chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzylamide

N-{4-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-benzyl}-2-hydroxy-acetamide

N-{4-[3-Chloro-4-(2,4-difluoro-benzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]-phenyl}-acetamide

{2-[3-Bromo-1-(2,6-difluoro-phenyl)-6-methyl-2-oxo-1,2-dihydro-pyridin-4-ylloxymethyl]-5-fluoro-benzyl}-carbamic acid ethyl ester

The above names were generated using ChemDraw Ultra version 6.0.2, which is put out by CambridgeSoft.com, Cambridge, MA; or ACD Namepro version 5.09, which is put out
5 by ACDlabs.com.

Definitions

As used herein, the term "alkenyl" refers to a straight or branched hydrocarbon of a designed number of carbon atoms containing at least one carbon-carbon double bond. Examples
10 of "alkenyl" include vinyl, allyl, and 2-methyl-3-heptene.

The term "alkoxy" represents an alkyl attached to the parent molecular moiety through an oxygen bridge. Examples of

alkoxy groups include, for example, methoxy, ethoxy, propoxy and isopropoxy.

The term "thioalkoxy" represents an alkyl attached to the parent molecular moiety through a sulfur atom. Examples of
5 thioalkoxy groups include, for example, thiomethoxy, thioethoxy, thiopropoxy and thioisopropoxy.

As used herein, the term "alkyl" includes those alkyl groups of a designed number of carbon atoms. Alkyl groups may be straight or branched. Examples of "alkyl" include methyl,
10 ethyl, propyl, isopropyl, butyl, iso-, sec- and tert-butyl, pentyl, hexyl, heptyl, 3-ethylbutyl, and the like. "Cx-Cy alkyl" represents an alkyl group of the specified number of carbons. For example, C₁-C₄ alkyl includes all alkyl groups that include at least one and no more than four carbon atoms.
15 It also contains subgroups, such as, for example, C₂-C₃ alkyl or C₁-C₃ alkyl.

The term "aryl" refers to an aromatic hydrocarbon ring system containing at least one aromatic ring. The aromatic ring may optionally be fused or otherwise attached to other
20 aromatic hydrocarbon rings or non-aromatic hydrocarbon rings. Examples of aryl groups include, for example, phenyl, naphthyl, 1,2,3,4-tetrahydronaphthalene, indanyl, and biphenyl. Preferred examples of aryl groups include phenyl and naphthyl. The most preferred aryl group is phenyl. The
25 aryl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. Thus, such aryl groups can be optionally substituted with groups such as, for example, C₁-C₆ alkyl, C₁-C₆ alkoxy, halogen, hydroxy, cyano, nitro, amino, mono- or di-(C₁-
30 C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono- or di(C₁-C₆)alkylamino(C₁-C₆)alkyl.

The term "arylalkyl" refers to an aryl group, as defined above, attached to the parent molecular moiety through an alkyl group, as defined above. Preferred arylalkyl groups include, benzyl, phenethyl, phenpropyl, and phenbutyl. More preferred arylalkyl groups include benzyl and phenethyl. The most preferred arylalkyl group is benzyl. The aryl portions of these groups are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. Thus, such aryl groups can be optionally substituted with groups such as, for example, C₁-C₆ alkyl, C₁-C₆ alkoxy, halogen, hydroxy, cyano, nitro, amino, mono- or di-(C₁-C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono- or di(C₁-C₆)alkylamino(C₁-C₆)alkyl.

The term "arylalkoxy" refers to an aryl group, as defined above, attached to the parent molecular moiety through an alkoxy group, as defined above. Preferred arylalkoxy groups include, benzyloxy, phenethyloxy, phenpropyloxy, and phenbutyloxy. The most preferred arylalkoxy group is benzyloxy.

The term "cycloalkyl" refers to a C₃-C₈ cyclic hydrocarbon. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl. More preferred cycloalkyl groups include cyclopropyl.

The term "cycloalkylalkyl," as used herein, refers to a C₃-C₈ cycloalkyl group attached to the parent molecular moiety through an alkyl group, as defined above. Examples of cycloalkylalkyl groups include cyclopropylmethyl and cyclopentylethyl.

The terms "halogen" or "halo" indicate fluorine, chlorine, bromine, or iodine.

The term "heterocycloalkyl," refers to a non-aromatic ring system containing at least one heteroatom selected from nitrogen, oxygen, and sulfur, wherein the non-aromatic heterocycle is attached to the core. The heterocycloalkyl ring may be optionally fused to or otherwise attached to other heterocycloalkyl rings, aromatic heterocycles, aromatic hydrocarbons and/or non-aromatic hydrocarbon rings. Preferred heterocycloalkyl groups have from 3 to 7 members. Examples of heterocycloalkyl groups include, for example, piperazine, 1,2,3,4-tetrahydroisoquinoline, morpholine, piperidine, tetrahydrofuran, pyrrolidine, and pyrazole. Preferred heterocycloalkyl groups include piperidinyl, piperazinyl, morpholinyl, and pyrrolidinyl. The heterocycloalkyl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. Thus, such heterocycloalkyl groups can be optionally substituted with groups such as, for example, C₁-C₆ alkyl, C₁-C₆ alkoxy, halogen, hydroxy, cyano, nitro, amino, mono- or di-(C₁-C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono- or di(C₁-C₆)alkylamino(C₁-C₆)alkyl.

The term "heteroaryl" refers to an aromatic ring system containing at least one heteroatom selected from nitrogen, oxygen, and sulfur. The heteroaryl ring may be fused or otherwise attached to one or more heteroaryl rings, aromatic or non-aromatic hydrocarbon rings or heterocycloalkyl rings. Examples of heteroaryl groups include, for example, pyridine, furan, thiophene, 5,6,7,8-tetrahydroisoquinoline and pyrimidine. Preferred examples of heteroaryl groups include thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, benzimidazolyl, furanyl, benzofuranyl, thiazolyl, benzothiazolyl, isoxazolyl, oxadiazolyl, isothiazolyl, benzisothiazolyl, triazolyl, tetrazolyl,

pyrrolyl, indolyl, pyrazolyl, and benzopyrazolyl. Preferred heteroaryl groups include pyridyl. The heteroaryl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. Thus, such heteroaryl groups can be optionally substituted with groups such as, for example, C₁-C₆ alkyl, C₁-C₆ alkoxy, halogen, hydroxy, cyano, nitro, amino, mono- or di-(C₁-C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono- or di(C₁-C₆)alkylamino(C₁-C₆)alkyl.

The term "heteroarylalkyl" refers to a heteroaryl group, as defined above, attached to the parent molecular moiety through an alkyl group, as defined above. Preferred heteroarylalkyl groups include, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, isoxazolemethyl, isoxazoleethyl, pyrazinemethyl and pyrazineethyl. More preferred heteroarylalkyl groups include pyridylmethyl and pyridylethyl. The heteroaryl portions of these groups are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. Thus, such heteroaryl groups can be optionally substituted with groups such as, for example, C₁-C₆ alkyl, C₁-C₆ alkoxy, halogen, hydroxy, cyano, nitro, amino, mono- or di-(C₁-C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono- or di(C₁-C₆)alkylamino(C₁-C₆)alkyl.

If two or more of the same substituents are on a common atom, e.g., di(C₁-C₆)alkylamino, it is understood that the nature of each group is independent of the other.

As used herein, the term "p38 mediated disorder" refers to any and all disorders and disease states in which p38 plays a role, either by control of p38 itself, or by p38 causing another factor to be released, such as but not limited to IL-

1, IL-6 or IL-8. A disease state in which, for instance, IL-1 is a major component, and whose production or action, is exacerbated or secreted in response to p38, would therefore be considered a disorder mediated by p38.

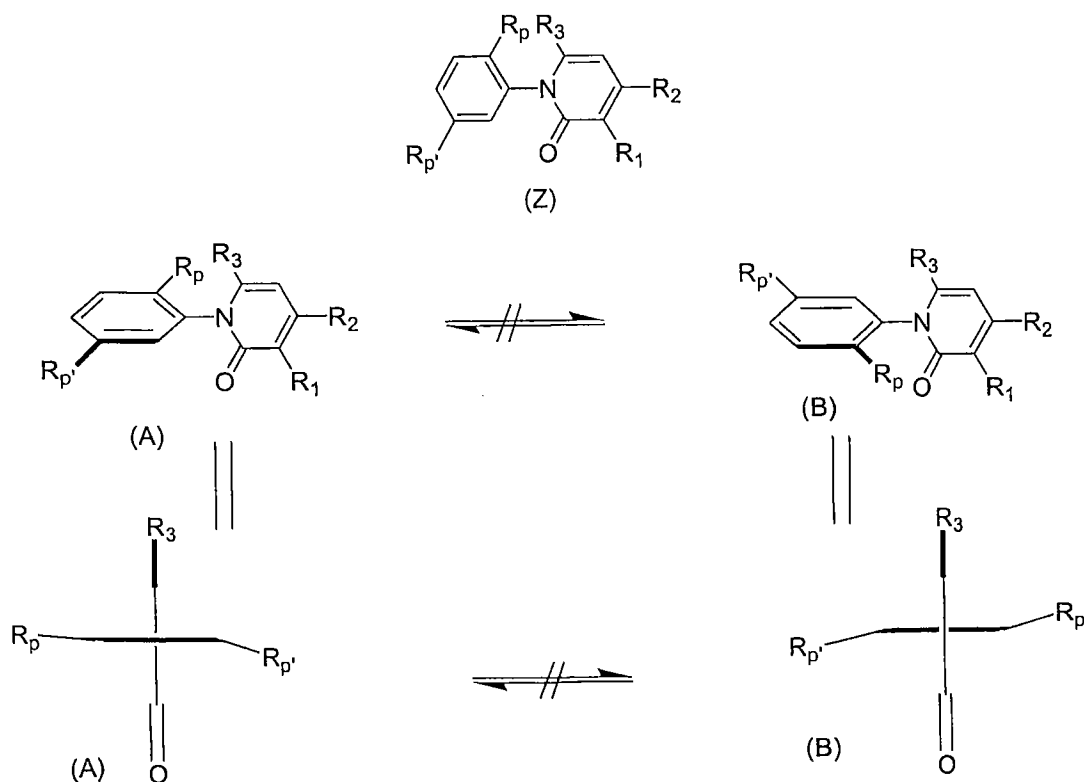
5 As TNF-beta has close structural homology with TNF-alpha (also known as cachectin), and since each induces similar biologic responses and binds to the same cellular receptor, the synthesis of both TNF-alpha and TNF-beta are inhibited by the compounds of the present invention and thus are herein
10 referred to collectively as "TNF" unless specifically delineated otherwise.

Non-toxic pharmaceutically acceptable salts include, but are not limited to salts of inorganic acids such as hydrochloric, sulfuric, phosphoric, diphosphoric, hydrobromic,
15 and nitric or salts of organic acids such as formic, citric, malic, maleic, fumaric, tartaric, succinic, acetic, lactic, methanesulfonic, p-toluenesulfonic, 2-hydroxyethylsulfonic, salicylic and stearic. Similarly, pharmaceutically acceptable cations include, but are not limited to sodium, potassium,
20 calcium, aluminum, lithium and ammonium. Those skilled in the art will recognize a wide variety of non-toxic pharmaceutically acceptable addition salts.

The compounds of this invention may contain one or more asymmetric carbon atoms, so that the compounds can exist in
25 different stereoisomeric forms. These compounds can be, for example, racemates, chiral non-racemic or diastereomers. In these situations, the single enantiomers, i.e., optically active forms, can be obtained by asymmetric synthesis or by resolution of the racemates. Resolution of the racemates can
30 be accomplished, for example, by conventional methods such as crystallization in the presence of a resolving agent; chromatography, using, for example a chiral HPLC column; or derivatizing the racemic mixture with a resolving reagent to

generate diastereomers, separating the diastereomers via chromatography or selective crystallization, and removing the resolving agent to generate the original compound in enantiomerically enriched form. Any of the above procedures
 5 can be repeated to increase the enantiomeric purity of a compound.

The compounds of the invention may exist as atropisomers, i.e., chiral rotational isomers. The invention encompasses
 10 the racemic and the resolved atropisomers. The following illustration generically shows a compound (Z) that can exist as atropisomers as well as its two possible atropisomers (A) and (B). This illustration also shows each of atropisomers (A) and (B) in a Fischer projection. In this illustration, R_1 ,
 15 R_2 , and R_4 carry the same definitions as set forth for Formula I, $R_{p'}$ is a substituent within the definition of R_5 , and R_p is a non-hydrogen substituent within the definition of R_5 .



When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless otherwise specified, it is intended that the compounds include the cis, trans, Z- and E- configurations. Likewise, all
5 tautomeric forms are also intended to be included.

The compounds of general Formula I may be administered orally, topically, parenterally, by inhalation or spray or rectally in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and
10 vehicles. The term parenteral as used herein includes percutaneous, subcutaneous, intravascular (e.g., intravenous), intramuscular, or intrathecal injection or infusion techniques and the like. In addition, there is provided a pharmaceutical formulation comprising a compound of general Formula I and a
15 pharmaceutically acceptable carrier. One or more compounds of general Formula I may be present in association with one or more non-toxic pharmaceutically acceptable carriers and/or diluents and/or adjuvants, and if desired other active ingredients. The pharmaceutical compositions containing
20 compounds of general Formula I may be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsion, hard or soft capsules, or syrups or elixirs.

For oral administration, the pharmaceutical composition
25 may be in the form of, for example, a tablet, hard or soft capsule, lozenges, dispensable powders, suspension, or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a particular amount of the active ingredient. Examples of such dosage units are tablets or
30 capsules.

Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may

contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preservative agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the
5 active ingredient in admixture with non-toxic pharmaceutically acceptable excipients that are suitable for the manufacture of tablets. These excipients may be for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating
10 agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatin or acacia, and lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques. In some cases such coatings may be prepared by
15 known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate may be employed.

20 Formulations for oral use may also be presented as hard gelatin capsules, wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate, or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil
25 medium, for example peanut oil, liquid paraffin or olive oil.

Formulations for oral use may also be presented as lozenges.

Aqueous suspensions contain the active materials in admixture with excipients suitable for the manufacture of
30 aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydropropyl-methylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia;

dispersing or wetting agents may be a naturally-occurring phosphatide, for example, lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose or saccharin.

Oily suspensions may be formulated by suspending the active ingredients in a vegetable oil, for example arachis oil, olive oil, sesame oil, or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin, or cetyl alcohol. Sweetening agents and flavoring agents may be added to provide palatable oral preparations. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents or suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring, and coloring agents, may also be present.

Pharmaceutical compositions of the invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil or a mineral oil or mixtures of these. Suitable emulsifying agents may be naturally-occurring gums, for example gum acacia or gum tragacanth, naturally-occurring phosphatides, for example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol, anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening and flavoring agents.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol, glucose or sucrose. Such formulations may also contain a demulcent, a preservative, and flavoring and coloring agents. The pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleaginous suspension. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents that have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parentally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

The compounds of general Formula I may also be administered in the form of suppositories, e.g., for rectal administration of the drug. These compositions can be

prepared by mixing the drug with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter and polyethylene glycols.

Compounds of general Formula I may be administered parenterally in a sterile medium. The drug, depending on the vehicle and concentration used, can either be suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives, and buffering agents can be dissolved in the vehicle.

The active ingredient may also be administered by injection (IV, IM, subcutaneous or jet) as a composition wherein, for example, saline, dextrose, or water may be used as a suitable carrier. The pH of the composition may be adjusted, if necessary, with suitable acid, base, or buffer. Suitable bulking, dispersing, wetting or suspending agents, including mannitol and PEG 400, may also be included in the composition. A suitable parenteral composition can also include a compound formulated as a sterile solid substance, including lyophilized powder, in injection vials. Aqueous solution can be added to dissolve the compound prior to injection.

For disorders of the eye or other external tissues, e.g., mouth and skin, the formulations are preferably applied as a topical gel, spray, ointment or cream, or as a suppository, containing the active ingredients in a total amount of, for example, 0.075 to 30% w/w, preferably 0.2 to 20% w/w and most preferably 0.4 to 15% w/w. When formulated in an ointment, the active ingredients may be employed with either paraffinic or a water-miscible ointment base.

Alternatively, the active ingredients may be formulated in a cream with an oil-in-water cream base. If desired, the

aqueous phase of the cream base may include, for example at least 30% w/w of a polyhydric alcohol such as propylene glycol, butane-1,3-diol, mannitol, sorbitol, glycerol, polyethylene glycol and mixtures thereof. The topical
5 formulation may desirably include a compound, which enhances absorption or penetration of the active ingredient through the skin or other affected areas. Examples of such dermal penetration enhancers include dimethylsulfoxide and related analogs. The compounds of this invention can also be
10 administered by a transdermal device. Preferably topical administration will be accomplished using a patch either of the reservoir and porous membrane type or of a solid matrix variety. In either case, the active agent is delivered continuously from the reservoir or microcapsules through a
15 membrane into the active agent permeable adhesive, which is in contact with the skin or mucosa of the recipient. If the active agent is absorbed through the skin, a controlled and predetermined flow of the active agent is administered to the recipient. In the case of microcapsules, the encapsulating
20 agent may also function as the membrane. The transdermal patch may include the compound in a suitable solvent system with an adhesive system, such as an acrylic emulsion, and a polyester patch. The oily phase of the emulsions of this invention may be constituted from known ingredients in a known manner.
25 While the phase may comprise merely an emulsifier, it may comprise a mixture of at least one emulsifier with a fat or oil or with both a fat and an oil. Preferably, a hydrophilic emulsifier is included together with a lipophilic emulsifier, which acts as a stabilizer. It is also preferred to include
30 both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make-up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called emulsifying ointment base, which forms the oily,

dispersed phase of the cream formulations. Emulsifiers and emulsion stabilizers suitable for use in the formulation of the present invention include Tween 60, Span 80, cetostearyl alcohol, myristyl alcohol, glyceryl monostearate, and sodium lauryl sulfate, among others. The choice of suitable oils or fats for the formulation is based on achieving the desired cosmetic properties, since the solubility of the active compound in most oils likely to be used in pharmaceutical emulsion formulations is very low. Thus, the cream should preferably be a non-greasy, non-staining and washable product with suitable consistency to avoid leakage from tubes or other containers. Straight or branched chain, mono- or dibasic alkyl esters such as di-isoadipate, isocetyl stearate, propylene glycol diester of coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of branched chain esters may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils can be used.

Formulations suitable for topical administration to the eye also include eye drops wherein the active ingredients are dissolved or suspended in suitable carrier, especially an aqueous solvent for the active ingredients. The anti-inflammatory active ingredients are preferably present in such formulations in a concentration of 0.5 to 20%, advantageously 0.5 to 10% and particularly about 1.5% w/w. For therapeutic purposes, the active compounds of this combination invention are ordinarily combined with one or more adjuvants appropriate to the indicated route of administration. If administered per os, the compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanolic acids, cellulose alkyl esters, talc, stearic acid, magnesium stearate, magnesium

oxide, sodium and calcium salts of phosphoric and sulfuric acids, gelatin, acacia gum, sodium alginate, polyvinylpyrrolidone, and/or polyvinyl alcohol, and then tableted or encapsulated for convenient administration. Such capsules or tablets may contain a controlled-release formulation as may be provided in a dispersion of active compound in hydroxypropylmethyl cellulose. Formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. These solutions and suspensions may be prepared from sterile powders or granules having one or more of the carriers or diluents mentioned for use in the formulations for oral administration. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil, cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, and/or various buffers. Other adjuvants and modes of administration are well and widely known in the pharmaceutical art.

The amount of therapeutically active compounds that are administered and the dosage regimen for treating a disease condition with the compounds and/or compositions of this invention depends on a variety of factors, including the age, weight, sex and medical condition of the subject, the severity of the inflammation or inflammation related disorder, the route and frequency of administration, and the particular compound employed, and thus may vary widely. The pharmaceutical compositions may contain active ingredients in the range of about 0.1 to 1000 mg, preferably in the range of about 7.0 to 350 mg. A daily dose of about 0.01 to 100 mg/kg body weight, preferably between about 0.1 and about 50 mg/kg body weight and most preferably between about 0.5 to 30 mg/kg body weight, may be appropriate. The daily dose can be administered in one to four doses per day. In the case of skin

conditions, it may be preferable to apply a topical preparation of compounds of this invention to the affected area two to four times a day.

It will be understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, and rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

For administration to non-human animals, the composition may also be added to the animal feed or drinking water. It may be convenient to formulate the animal feed and drinking water compositions so that the animal takes in a therapeutically appropriate quantity of the composition along with its diet. It may also be convenient to present the composition as a premix for addition to the feed or drinking water.

The disclosures in this application of all articles and references, including patents, are incorporated herein by reference.

The invention is illustrated further by the following examples, which are not to be construed as limiting the invention in scope or spirit to the specific procedures described in them.

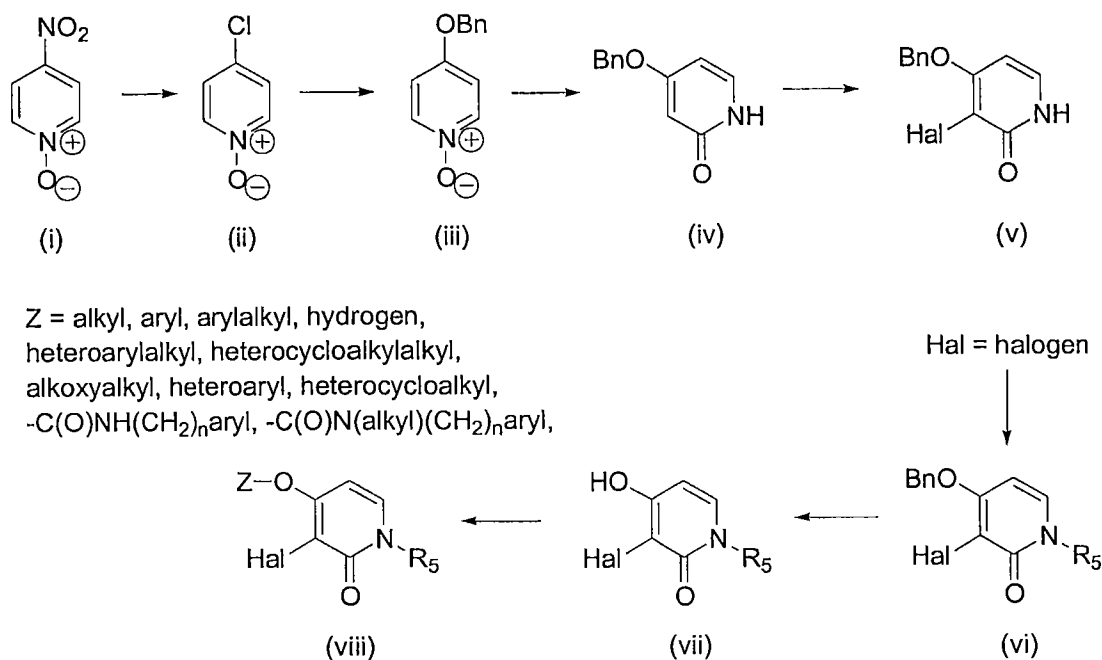
The starting materials and various intermediates may be obtained from commercial sources, prepared from commercially available compounds, or prepared using well-known synthetic methods.

The compound names in this application were created using ACD Name Pro version 5.09, or ChemDraw ultra version 6.0.2, software.

General Synthetic Procedures

Representative procedures for the preparation of compounds of the invention are outlined below in the Schemes. The starting materials can be purchased or prepared using methods known to those skilled in the art. Similarly, the preparation of the various intermediates can be achieved using methods known in the art. The starting materials may be varied and additional steps employed to produce compounds encompassed by the invention, as demonstrated by the examples below. In addition, different solvents and reagents can typically be used to achieve the above transformations. Protection of reactive groups may also be necessary to achieve the above transformations. In general, the need for protecting groups, as well as the conditions necessary to attach and remove such groups, will be apparent to those skilled in the art of organic synthesis. When a protecting group is employed, deprotection will generally be required. Suitable protecting groups and methodology for protection and deprotection such as those described in *Protecting Groups in Organic Synthesis* by Greene and Wuts are known and appreciated in the art.

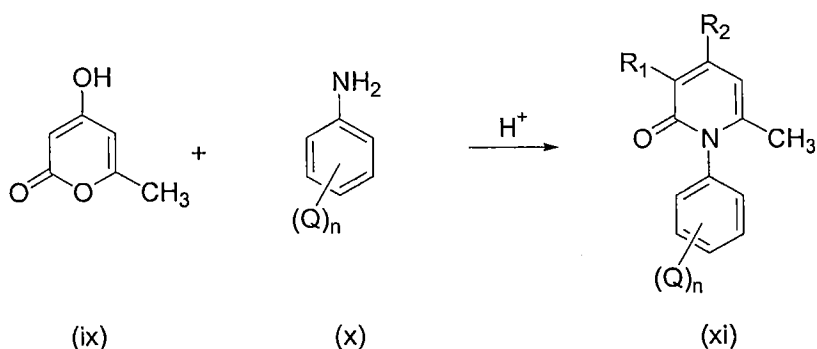
Scheme 1



In this scheme, R_5 is as defined above.

- 5 Alternatively, the compounds of the instant invention can be prepared according to the method outlined in Scheme 2.

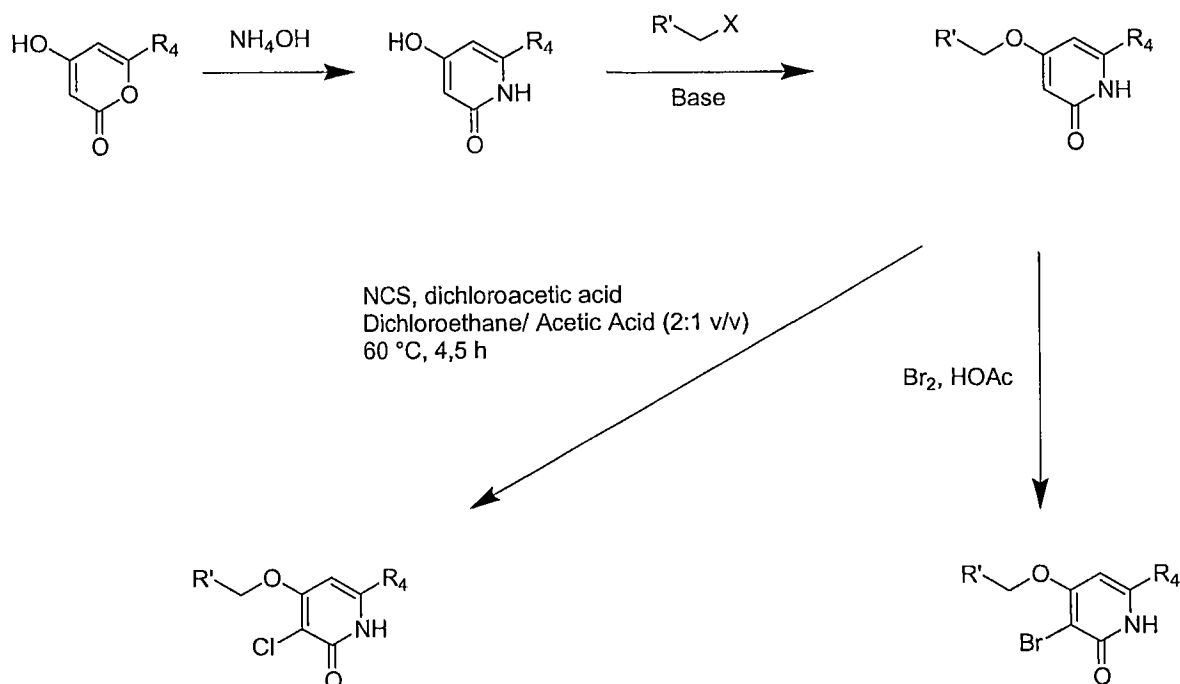
Scheme 2



- 10 In Scheme 2, Q at each occurrence is independently alkyl, halogen, alkoxy, arylalkoxy, thioalkoxy, alkoxycarbonyl, arylalkoxycarbonyl, CO_2H , CN, amidinoxime, NR_6R_7 , $NR_6R_7\text{alkyl}$, $-C(O)NR_6R_7$, amidino, haloalkyl, or haloalkoxy; and n is 0, 1, 2, 3, 4, or 5.

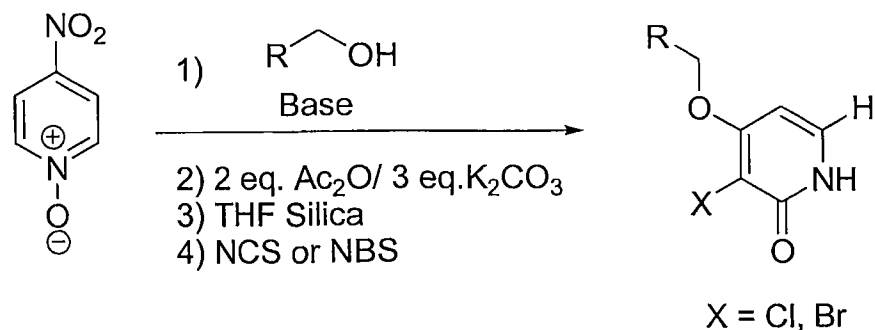
Alternatively, compounds of the invention can be prepared using the procedures outlined in Schemes 3-25. In Schemes 3-25, the X, X', R, R', and R'' substituents on groups such as aryl, heteroaryl, amine, and alkyl, carry the same definition
 5 described above for substituents on these groups.

Scheme 3

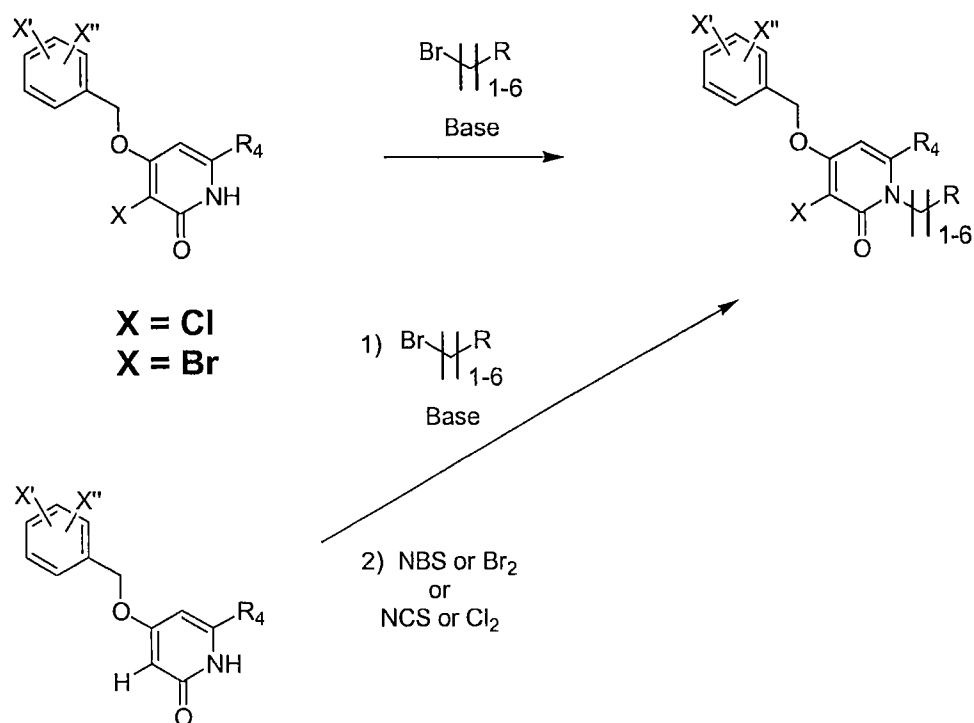


10

Scheme 4

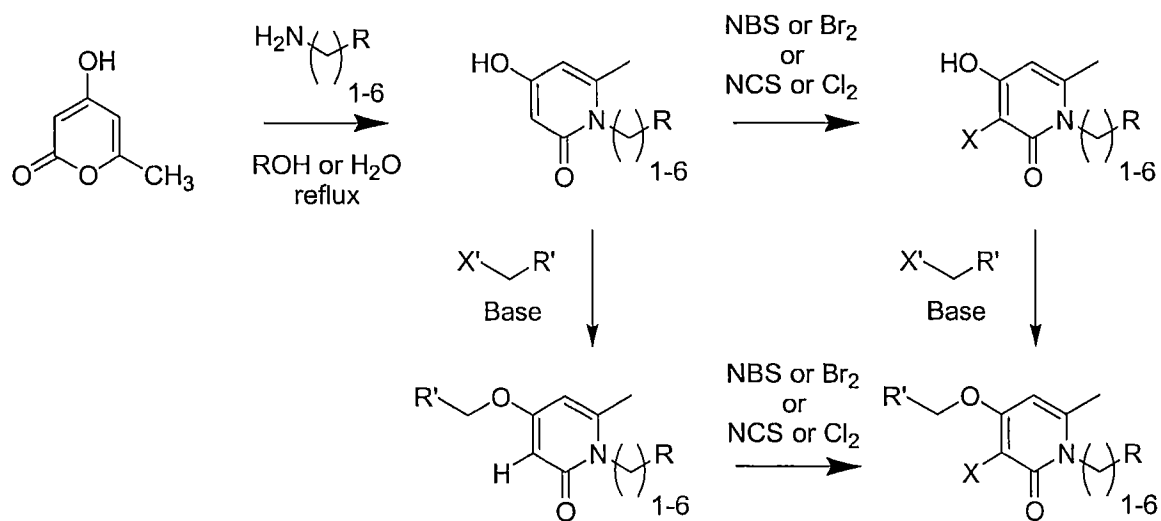


Scheme 5



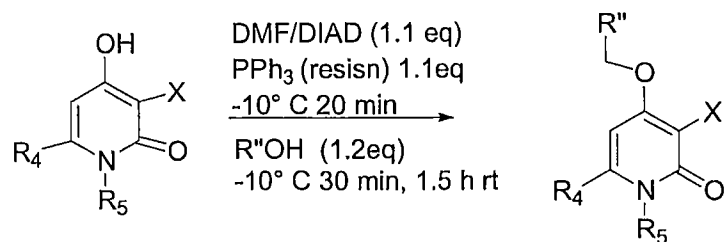
5

Scheme 6



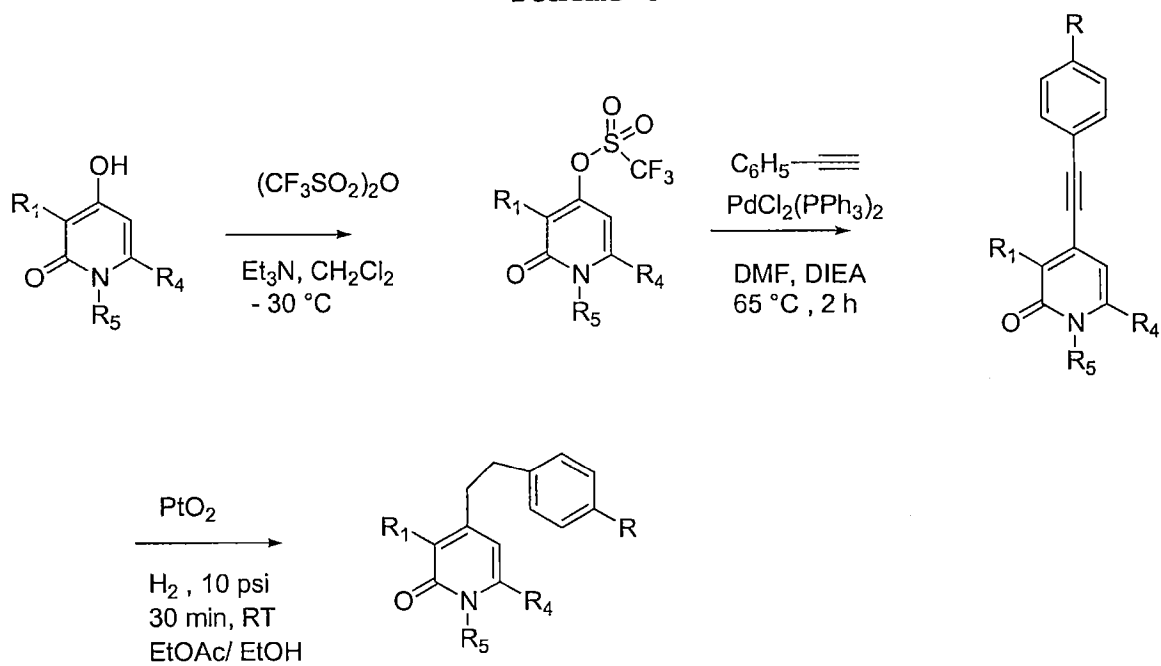
Scheme 7

10



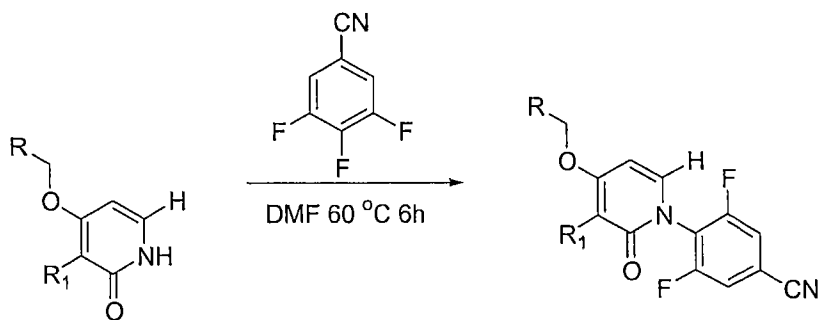
PPh₃ resin 3 mmol=1 g PPh₃

Scheme 8



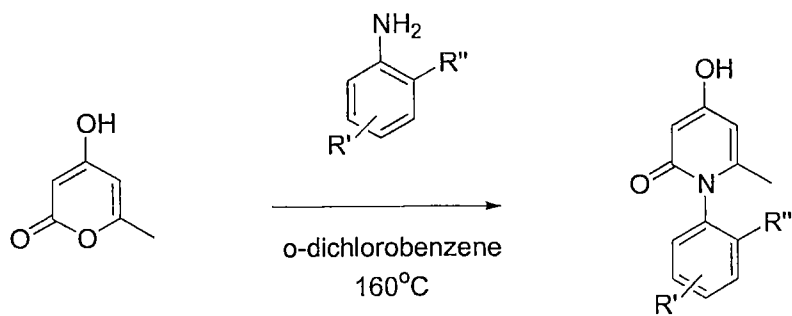
5

Scheme 9



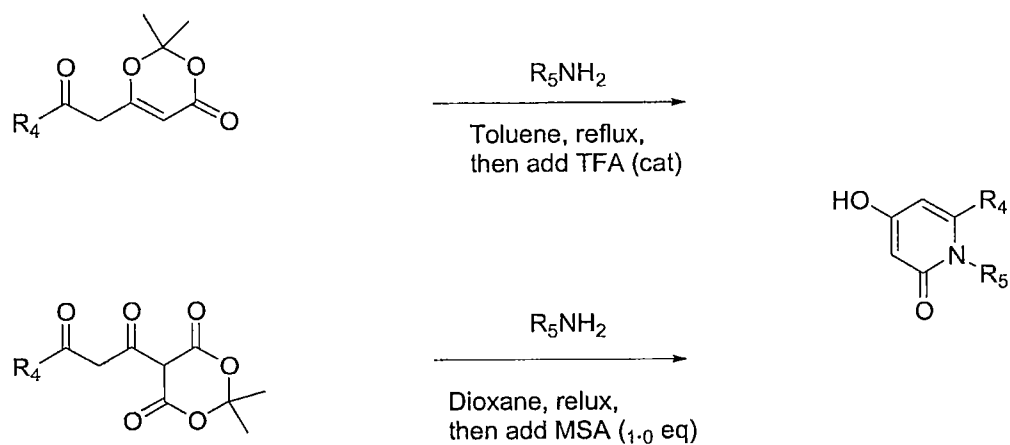
10

Scheme 10



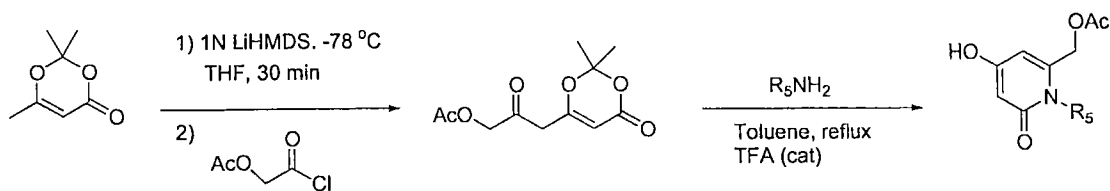
5

Scheme 11

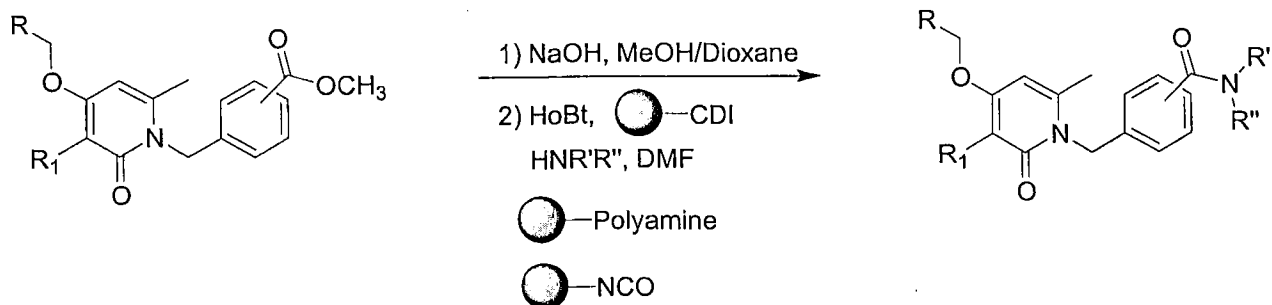


Scheme 12

10

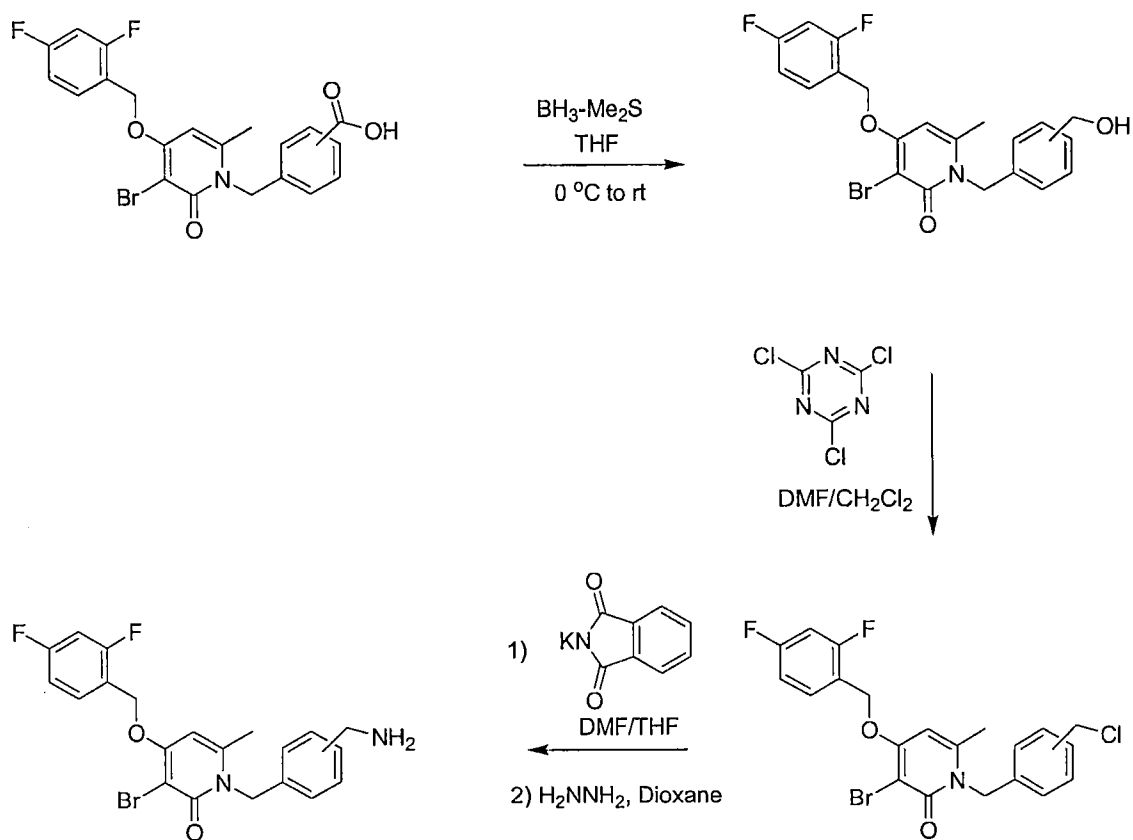


Scheme 13



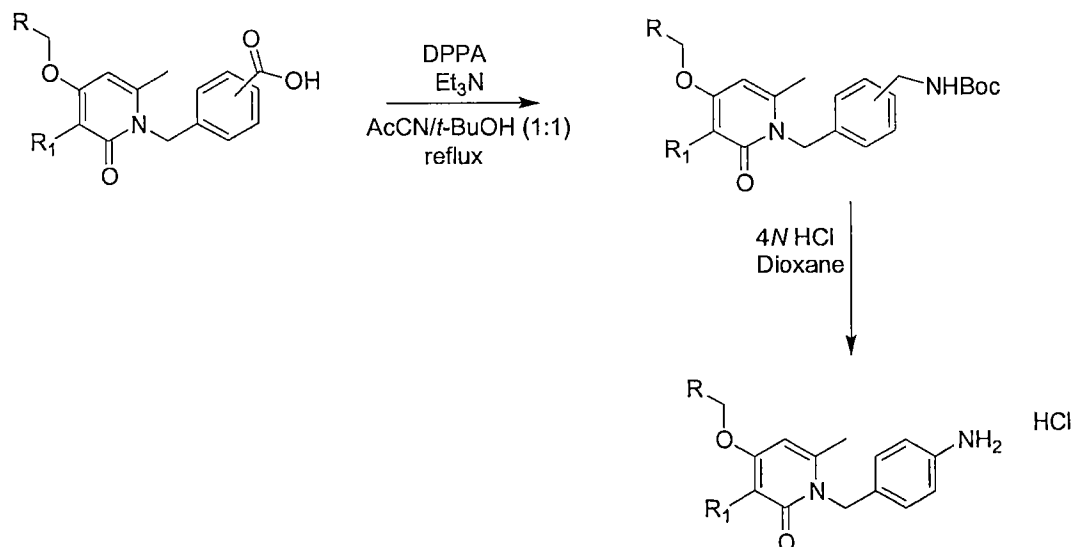
15

Scheme 14

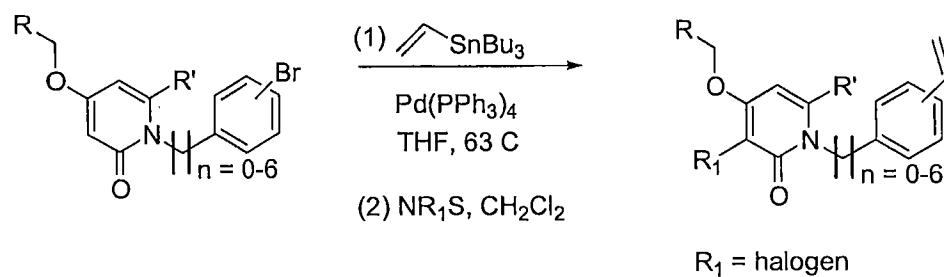


5

Scheme 15

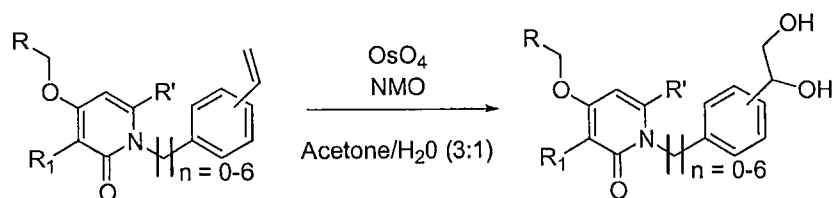


Scheme 16



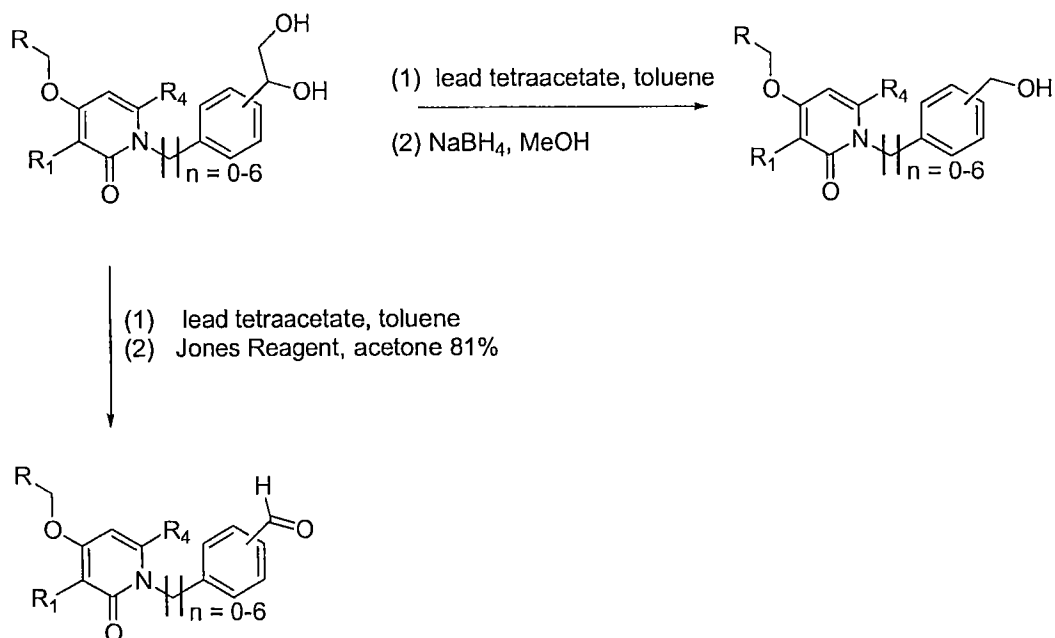
5

Scheme 17

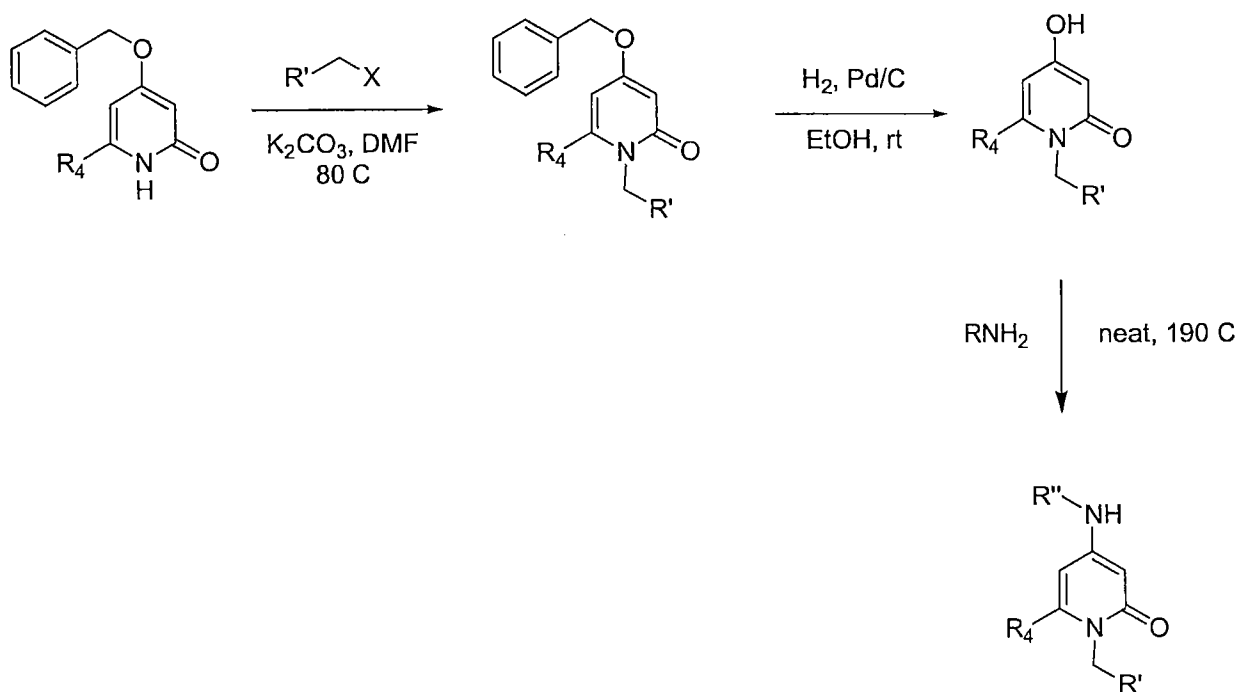


Scheme 18

10

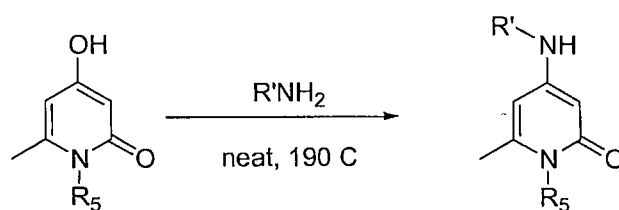


Scheme 19



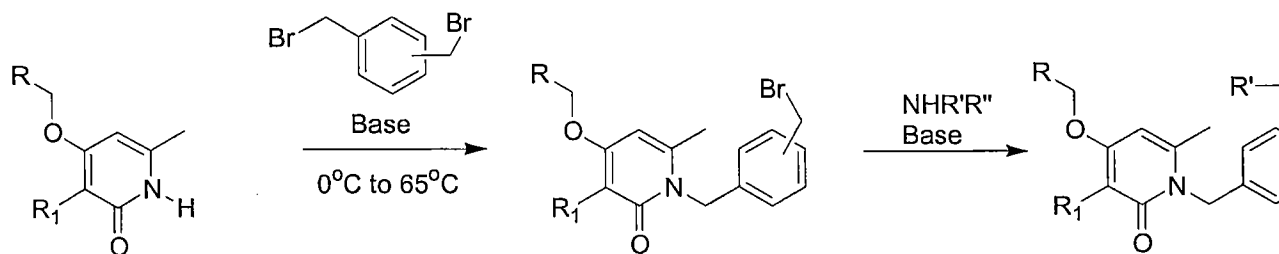
5

Scheme 20



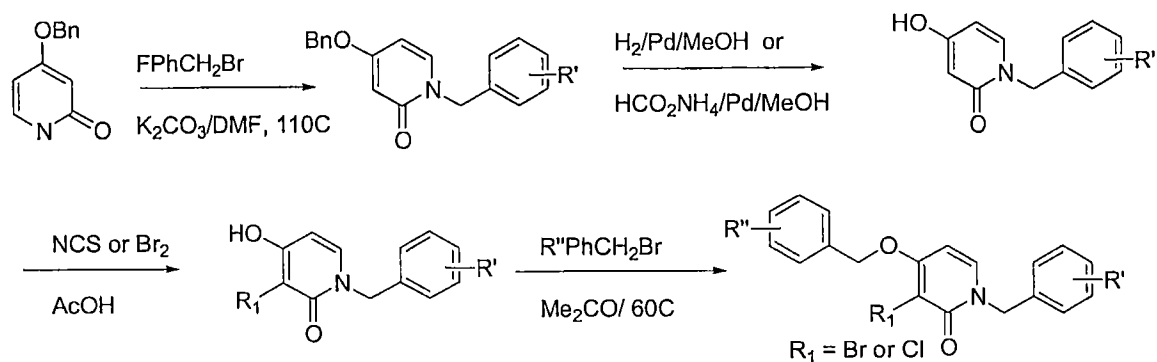
10

Scheme 21



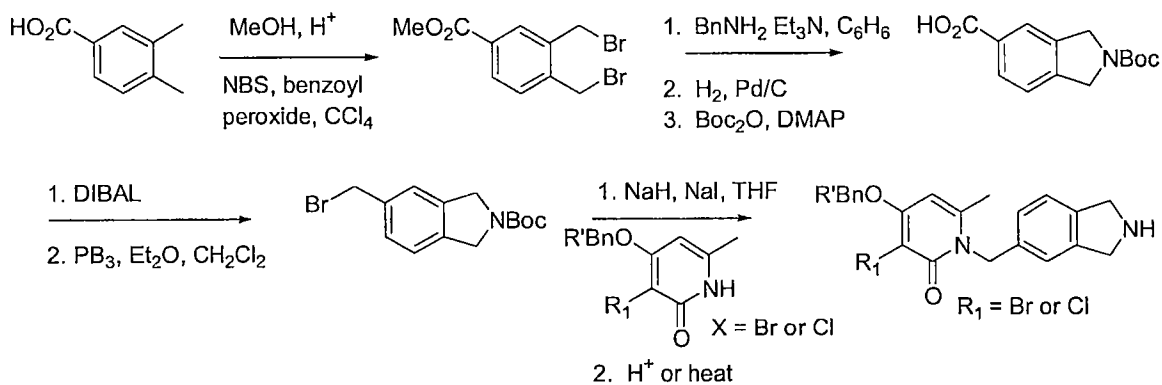
15

Scheme 22



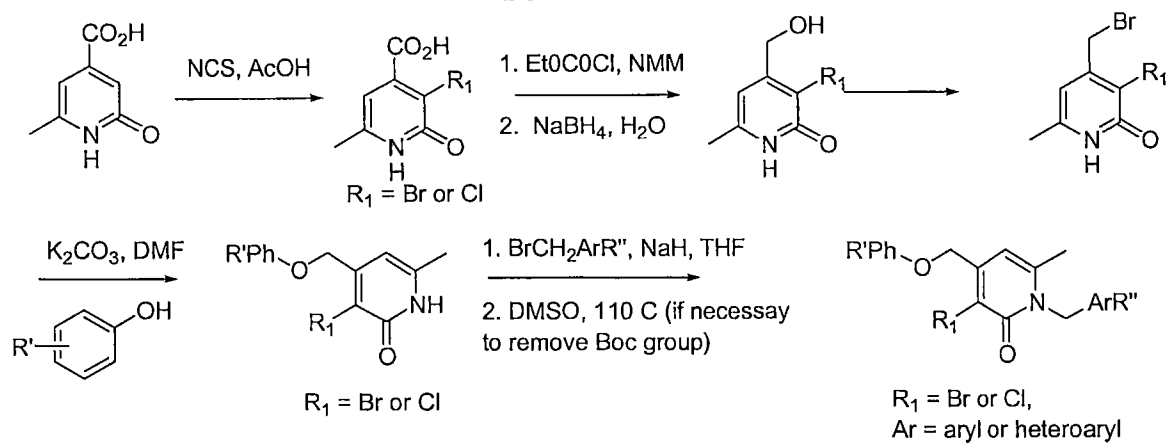
5

Scheme 23

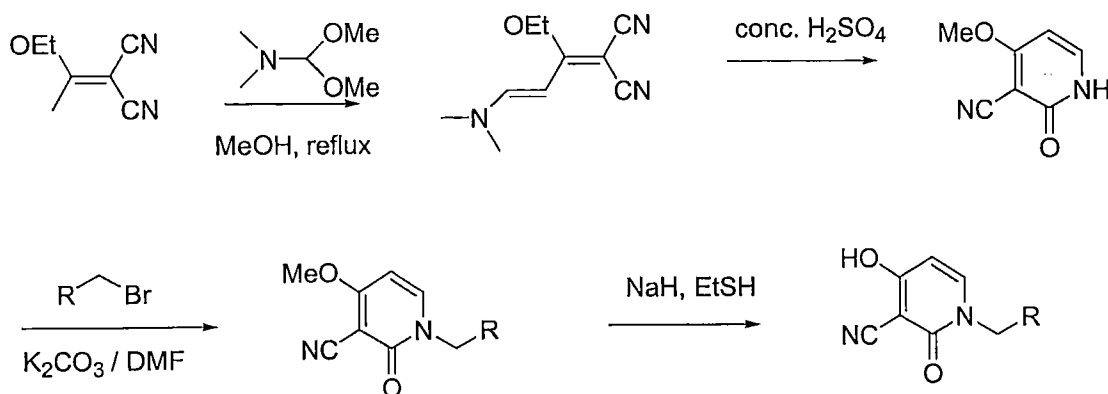


10

Scheme 24



Scheme 25



5

The invention is illustrated further by the following examples, which are not to be construed as limiting the invention in scope or spirit to the specific procedures described in them. Those having skill in the art will recognize that the starting materials may be varied and additional steps employed to produce compounds encompassed by the invention, as demonstrated by the following examples. Those skilled in the art will also recognize that it may be necessary to utilize different solvents or reagents to achieve some of the above transformations. In some cases, protection of reactive functionalities may be necessary to achieve the above transformations. In general, such need for protecting groups, as well as the conditions necessary to attach and remove such groups, will be apparent to those skilled in the art of organic synthesis. When a protecting group is employed, a deprotection step may be required. Suitable protecting groups and methodology for protection and deprotection such as those described in *Protecting Groups in Organic Synthesis* by Greene and Wuts are well known and appreciated in the art.

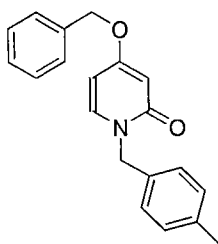
Unless otherwise specified, all reagents and solvents are of standard commercial grade and are used without further

purification. The appropriate atmosphere to run the reaction under, for example, air, nitrogen, hydrogen, argon and the like, will be apparent to those skilled in the art.

5 Examples

Example 1

4-(benzyloxy)-1-(4-methylbenzyl)pyridin-2(1H)-one



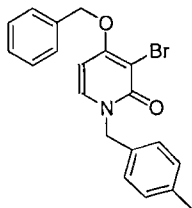
10

4-Benzyloxy-2(1H)-pyridone (3.0 g, 0.015 mol), 4-methylbenzyl bromide (3.15 g, 0.17 mol), and potassium carbonate (3.0 g, 0.022 mol) were heated at 80 °C for 2 hours. Contents were allowed to cool, diluted with water and a solid
15 (5.52 g) was filtered. FABHRMS m/z 306.1494 (M+H, C₂₀H₂₀NO₂ requires 306.1494). ¹H NMR (CDCl₃ /300 MHz): 7.50-7.40 (m, 5H); 7.20-7.05 (m, 5H); 6.07-6.00 (m, 1H); 5.95-5.90 (m, 1H); 5.05 (s, 2H); 5.00 (s, 2H); 2.32 (s, 3H).

Anal. Calcd for C₂₀H₁₉NO₂: C, 78.66; H, 6.27; N, 4.59.
20 Found: C, 78.54; H, 6.38; N, 4.58.

Example 2

4-(benzyloxy)-3-bromo-1-(4-methylbenzyl)pyridin-2(1H)-one

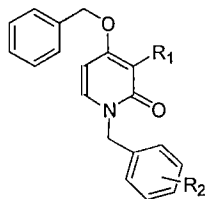


25

The material prepared in Example 1 (2.1 g, 0.007 mol) and sodium acetate (738 mg, 0.009 mol) in glacial acetic acid (15 mL) were cooled to 15 °C. Bromine (0.412 mL, 0.008) in glacial acetic acid (5 mL) was added dropwise. Contents were stirred
 5 2 hours, coming to room temperature. Water (200 mL) was added and a light yellow solid was filtered. Mp 150.4 - 151.2°C. FABHRMS m/z 384.0599 (M+H, C₂₀H₁₉BrNO₂ requires 384.0601). ¹H NMR (CDCl₃/300 MHz) δ: 7.42-7.30 (m, 5H); 7.22-7.08 (m, 5H); 6.02 (d, 1H); 5.20 (s, 2H); 5.12 (s, 2H); 2.32 (s, 3H).

10 Anal. Calcd for C₂₀H₁₈BrNO₂: C, 62.51; H, 4.72; N, 3.65. Found: C, 62.11; H, 4.48; N, 3.54.

Examples 3-10



15 The compounds of Examples 3-10 are prepared essentially according to the procedure set forth above with respect to Example 1. Compounds wherein R₁ = Br are prepared essentially according to the procedure of Example 2.

Example No.	R ₁	R ₂	MF	M+H m/z Requires	FABHRMS m/z
Ex. 3	-H	4-Br	C ₁₉ H ₁₆ BrNO ₂	370.0428	370.0443
Ex. 4	-Br	4-Br	C ₁₉ H ₁₅ Br ₂ NO ₂	447.9522	447.9548
Ex. 5	-H	4-Cl	C ₁₉ H ₁₆ ClNO ₂	326.0948	326.0893
Ex. 6	-Br	4-Cl	C ₁₉ H ₁₅ BrClNO ₂	404.0053	404.0035
Ex. 7	-H	3-F	C ₁₉ H ₁₆ FNO ₂	310.1243	310.1226
Ex. 8	-Br	3-F	C ₁₉ H ₁₅ BrFNO ₂		
Ex. 9	-H	2-F	C ₁₉ H ₁₆ FNO ₂	310.1231	310.1243

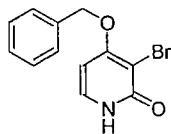
Ex. 10	-Br	2-F	C ₁₉ H ₁₅ BrFNO ₂	388.0348	388.0373
--------	-----	-----	--	----------	----------

NMR characterization of compounds of Examples 3-10

Ex. No.	NMR Data
Ex. 3	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.43 (d, 2H); 7.40-7.33 (m, 5H); 7.20-7.07 (m, 3H); 6.04-6.01 (m, 1H); 6.00-5.92 (m, 1H); 5.03 (s, 2H); 4.98 (s, 2H)
Ex. 4	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.50-7.15 (m, 10H); 6.06 (d, 1H); 5.20 (s, 2H), 5.10 (s, 2H)
Ex. 5	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.40-7.32 (m, 5H); 7.24 (AB quartet, 4H); 7.10 (d, 1H); 6.03-6.00 (m, 1H); 5.98-5.92 (m, 1H); 5.03 (s, 2H); 4.99 (s, 2H)
Ex. 6	¹ H NMR (CDCl ₃ /300 MHz): 7.43-7.20 (m, 10H); 6.08 (d, 1H); 5.20 (s, 2H); 5.10 (s, 2H)
Ex. 7	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.45-7.25 (m, 5H); 7.12 (d, 1H); 7.07-6.93 (m, 4H); 6.04-6.02 (m, 1H); 6.00-5.94 (m, 1H); 5.08 (s, 2H); 5.00 (s, 2H)
Ex. 8	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.43-7.25 (m, 6H); 7.21 (d, 1H); 7.10-6.93 (m, 3H); 6.08 (d, 1H); 5.22 (s, 2H); 5.12 (s, 2H)
Ex. 9	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.43-7.00 (m, 10H); 6.01-5.92 (m, 2H); 5.10 (s, 2H); 4.99 (s, 2H)
Ex. 10	¹ H NMR (CDCl ₃ /300 MHz): 7.52 (d of t, 1H); 7.44-7.26 (m, 7H); 7.15-7.00 (m, 2H); 6.03 (d, 1H); 5.20 (s, 2H); 5.15 (s, 2H)

Example 11

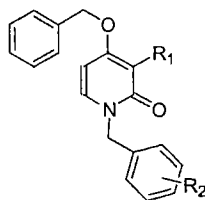
5 4-(benzyloxy)-3-bromopyridin-2(1H)-one



The material of Example 11 was prepared according to the procedure of Example 2. ¹H NMR (CDCl₃/300 MHz) δ: 7.50-7.30 (m, 6H); 6.20 (d, 1H); 5.24 (s, 2H).

10 Anal. Calcd for C₁₂H₁₀BrNO₂ (0.3H₂O): C, 50.48; H, 3.74; N, 4.91. Found: C, 50.79; H, 3.41; N, 4.82.

Examples 12-19



The compounds of Examples 12-19 are prepared essentially according to the procedures set forth above for Example 1. Compounds wherein $R_1 = \text{Br}$ are prepared essentially according to the procedure of Example 2.

5

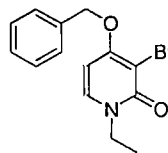
Example No.	R_1	R_2	MF	M+H Requires	FABHRMS m/z
Ex. 12	-Br	4-benzyloxy	$\text{C}_{26}\text{H}_{22}\text{BrNO}_3$	476.0861	476.0854
Ex. 13	-H	4-CO ₂ Me	$\text{C}_{21}\text{H}_{19}\text{NO}_4$	350.1392	350.1391
Ex. 14	-Br	4-CO ₂ Me	$\text{C}_{21}\text{H}_{18}\text{BrNO}_4$	428.0497	428.0480
Ex. 15	-Br	4-CO ₂ H	$\text{C}_{20}\text{H}_{16}\text{BrNO}_4$	414.0341	414.0360
Ex. 16	-H	4-CN	$\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_2$	317.1290	317.1270
Ex. 17	-Br	4-CN	$\text{C}_{20}\text{H}_{15}\text{BrN}_2\text{O}_2$	395.0395	395.0376
Ex. 18	-H	4-tButyl	$\text{C}_{23}\text{H}_{25}\text{NO}_2$	348.1964	348.1949
Ex. 19	-Br	4-tButyl	$\text{C}_{23}\text{H}_{24}\text{BrNO}_2$	426.1069	426.1023

NMR characterization of compounds of Examples 12-19

Ex. No.	NMR Data
Ex. 12	¹ H NMR (CDCl ₃ /300 MHz): 7.45-7.15 (m, 13H); 6.92 (d, 2H); 6.01 (d, 1H); 5.20 (s, 2H); 5.08 (s, 2H); 5.03 (s, 2H)
Ex. 13	¹ H NMR (CDCl ₃ /300 MHz): 8.00 (d, 2H); 7.40-7.25 (m, 7H); 7.10 (d, 1H); 6.03-6.01 (m, 1H); 6.00-5.93 (m, 1H); 5.12, (s, 2H); 5.00 (s, 2H); 3.95 (s, 3H)
Ex. 14	¹ H NMR (CDCl ₃ /300 MHz): 8.00 (d, 2H); 7.42-7.31 (m, 7H); 7.23 (d, 1H); 6.08 (d, 1H); 5.22 (d, 2H); 5.20 (s, 2H); 3.95 (s, 3H)
Ex. 15	¹ H NMR (DMSO-d ₆ /300 MHz): 8.00-7.80 (m, 3H); 7.53-7.27 (m, 7H); 6.50 (d, 1H); 5.32 (s, 2H); 5.20 (s, 2H)
Ex. 16	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.60 (d, 2H); 7.42-7.30 (m, 7H); 7.13 (d, 1H); 6.05-5.98 (m, 2H); 5.11 (s, 2H); 5.00 (s, 2H)
Ex. 17	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.61 (d, 2H); 7.48-7.30 (m, 6H); 7.23 (d, 2H); 6.12 (d, 1H); 5.22 (s, 2H); 5.20 (s, 2H)
Ex. 18	¹ H NMR (CDCl ₃ /300 MHz): 7.40-7.28 (m, 7H); 7.20 (d, 2H); 7.10 (d, 1H); 6.02 (d, 1H); 5.97-5.90 (m, 1H); 5.02 (d, 2H); 4.98 (d, 2H)
Ex. 19	¹ H NMR (CDCl ₃ /300 MHz) δ: 7.43-7.20 (m, 10H); 6.02 (d, 1H); 5.20 (s, 2H); 5.10 (s, 2H); 1.30 (s, 9H)

Example 20

4-(benzyloxy)-3-bromo-1-ethylpyridin-2(1H)-one

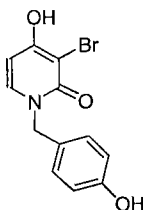


To 4-benzyloxy-2(1H)-pyridone (1.0 g, 0.005 mol) and potassium carbonate (1.0 g, 0.007 mol) in DMF (10 mL) was added bromoethane (0.82 mL, 0.011 mol). Contents were heated at 75°C overnight. Contents were allowed to cool and partitioned between EtOAc and water. The EtOAc layer was dried over MgSO₄, filtered, and concentrated in vacuo leaving a waxy solid, which was recrystallized from EtOAc/hexanes to give a white solid (720 mg). To the white solid (700 mg, 0.003 mol) in glacial acetic acid (10 mL), bromine (0.17 mL, 0.00325 mol) in glacial acetic acid (5 mL) was added dropwise at 15°C. Contents were stirred one hour at room temperature and a yellow solid (1.1 g) was filtered. The solid was partitioned between EtOAc and 2.5N sodium hydroxide. The EtOAc layer was dried over MgSO₄, filtered, and concentrated in vacuo leaving a colorless oil (710 mg), which solidified. FABHRMS m/z 310.0267 (M+H, C₁₄H₁₅BrNO₂ requires 310.0263). ¹H NMR (CDCl₃/300 MHz) δ: 7.45-7.30 (m, 6H); 7.22 (d, 1H); 6.07 (d, 1H); 5.20 (s, 2H); 4.00 (q, 2H); 1.32 (t, 3H).

Anal. Calcd for C₁₄H₁₄BrNO₂: C, 54.56; H, 4.58; N, 4.55. Found: C, 54.21; H, 4.38; N, 4.43.

Example 21

3-bromo-4-hydroxy-1-(4-hydroxybenzyl)pyridin-2(1H)-one

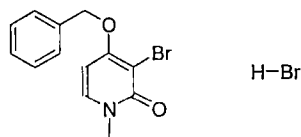


The material of Example 12 (120 mg, 0.25 mmol) and 10% palladium/carbon (30 mg) in glacial acetic acid (2 mL) were shaken at 55 lbs of hydrogen for 4 hours. Contents were filtered and the filtrate was concentrated *in vacuo* leaving an oil. FABHRMS m/z 295.9952 ($M+H$, $C_{12}H_{11}BrNO_3$ requires 295.9922). 1H NMR ($DMSO-d_6$ /300 MHz) δ : 11.40 (br s, 1H); 9.40 (br s, 1H); 7.60 (d, 1H); 7.10 (d, 2H); 6.70 (d, 2H); 6.02 (d, 1H); 4.93 (s, 2H).

Anal. Calcd for $C_{12}H_{10}BrNO_3$ ($1.4 H_2O$): C, 44.85; H, 4.02; N, 4.36. Found: C, 45.07; H, 4.10; N, 4.35.

Example 22

4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one
hydrobromide



15

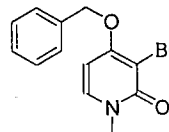
To 4-benzyloxy-2(1H)-pyridone (1.0 g, 0.005 mol) and potassium carbonate (760 mg, 0.0055 mol) in DMF (10 mL) was added methyl iodide (0.342 mL, 0.0055 mol). Contents were stirred overnight. Contents were partitioned between EtOAc and water. The EtOAc layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* leaving a white solid (960 mg).

To the white solid (332 mg, 0.0015 mol) in glacial acetic acid (10 mL), bromine (256 mg, 0.0016 mol) in glacial acetic acid (5 mL) was added dropwise at $15^\circ C$. Contents were stirred one hour at room temperature and the desired was filtered as a white solid, 262 mg (59% yield). mp $105.3-105.6^\circ C$. FABHRMS m/z 296.0097 ($M+H$, $C_{13}H_{13}BrNO_2$ requires 296.0110). 1H NMR ($CDCl_3$ /300 MHz) δ : 7.45-7.30 (m, 6H); 7.22 (d, 1H); 6.07 (d, 1H); 5.20 (s, 2H); 4.00 (q, 2H); 1.32 (t, 3H).

Anal. Calcd for $C_{13}H_{12}BrNO_2$ (HBr, $0.3H_2O$): C, 41.04; H, 3.60; N, 3.68. Found: C, 41.00; H, 3.87; N, 3.52.

Example 23

5 4-(benzyloxy)-3-bromo-1-methylpyridin-2(1H)-one

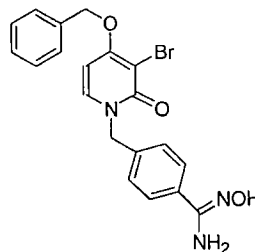


The material of Example 22 was partitioned between EtOAc and 2.5N sodium hydroxide. The EtOAc layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* leaving a red oil,
10 which solidified. FABHRMS m/z 294.0112 ($M+H$, $C_{13}H_{13}BrNO_2$ requires 294.0130). 1H NMR ($CDCl_3/300$ MHz): 7.45-7.30 (m, 6H); 7.22 (d, 1H); 6.07 (d, 1H); 5.20 (s, 2H); 4.00 (q, 2H); 1.32 (t, 3H).

Anal. Calcd for $C_{13}H_{12}BrNO_2$: C, 53.08; H, 4.11; N, 4.76.
15 Found: C, 53.06; H, 4.20; N, 4.74.

Example 24

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}-
 N' -hydroxybenzenecarboximidamide



20

The material of Example 17 (500 mg, 0.00127 mol), hydroxylamine hydrochloride (90 mg, 0.0013 mol) and sodium bicarbonate (109 mg) were refluxed in ethanol (15 mL) overnight. Contents were allowed to cool and a solid was
25 filtered and washed with water to give the desired as a white solid, 447 mg, (82% yield). mp 210.2-212.2 °C FABHRMS m/z 428.0634 ($M+H$, $C_{20}H_{19}BrN_3O_3$ requires 428.0610). 1H NMR ($DMSO-d_6$

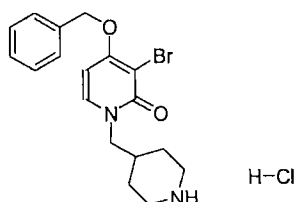
/ 300 MHz): 9.66 (s, 1H); 7.98 (d, 1H); 7.65 (d, 2H); 7.55-7.35 (m, 5H); 7.30 (d, 2H); 6.54 (d, 1H); 5.82 (s, 2H); 5.35 (s, 2H); 5.17 (s, 2H).

Anal. Calcd for $C_{20}H_{18}BrN_3O_3$: C, 56.09; H, 4.24; N, 9.81.

5 Found: C, 55.92; H, 4.01; N, 9.52.

Example 25

4-(benzyloxy)-3-bromo-1-(piperidin-4-ylmethyl)pyridin-2(1H)-one hydrochloride

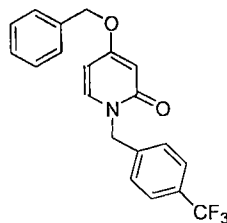


10

To the material of Example 11 (924 mg, 0.0033 mol) in DMF (5 mL) was added dropwise sodium bis(trimethylsilyl)amide (1M in THF, 3.6 mL). Contents were stirred one hour before adding dropwise a solution of 4-methanesulfonyloxymethyl-1-piperidine-1-carboxylic acid tert-butyl ester (*J. Labelled*
 15 *Compd, Radiopharm*, 38(7), 1996, 595-606) (1.0 g, 0.0036 mol) in DMF (5 mL). Contents were heated at 75°C overnight. Contents were allowed to cool and poured into water (100 mL). A solid was filtered and recrystallized from EtOAc to give
 20 white crystals (546 mg). The white crystals were refluxed in 4 N HCl/dioxane (10 mL) for 3 hours, allowed to cool and filtered to give the desired as a white solid, 415 mg (30% yield). mp 207.9°C. FABHRMS m/z 377.0852 ($M+H$, $C_{18}H_{23}BrClN_2O_2$ requires 377.0865). 1H NMR (DMSO- d_6 /300 MHz) δ : 8.90 (br, 1H);
 25 8.64 (br, 1H); 7.80 (d, 1H); 7.50-7.30 (m, 5H); 6.48 (d, 1H); 5.30 (s, 2H); 3.83 (d, 2H); 3.20 (d, 2H); 2.88-2.64 (m, 2H); 2.10-1.90 (m, 1H); 1.60 (d, 2H); 1.50-1.40 (m, 2H).
 Anal. Calcd for $C_{18}H_{22}BrClN_2O_2$ (0.3 H_2O): C, 51.58; H, 5.43; N, 6.68. Found: C, 51.59; H, 5.42; N, 6.81.

Example 26

4-(benzyloxy)-1-[4-(trifluoromethyl)benzyl]pyridin-2(1H)-one



5

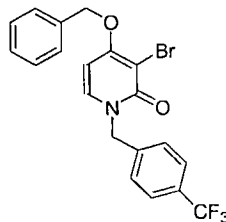
The material of Example 26 was prepared according to the procedure of Example 1. FABHRMS m/z 360.1213 ($M+H$, $C_{20}H_{17}F_3NO_2$ requires 360.1211). 1H NMR ($CDCl_3/300$ MHz) δ : 7.60 (d, 2H); 7.41-7.30 (m, 7H); 7.13 (d, 1H); 6.05-6.01 (m, 1H); 6.00-5.95 (m, 1H); 5.13 (s, 2H); 5.00 (s, 2H).

10

Anal. Calcd for $C_{20}H_{16}F_3NO_2$: C, 66.85; H, 4.49; N, 3.90. Found: C, 66.64; H, 4.26; N, 3.93.

Example 27

4-(benzyloxy)-3-bromo-1-[4-(trifluoromethyl)benzyl]pyridin-2(1H)-one



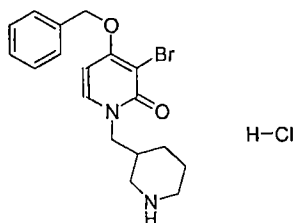
15

The material of Example 27 was prepared according to the procedure of Example 2. FABHRMS m/z 438.0308 ($M+H$, $C_{20}H_{15}BrF_3NO_2$ requires 438.0316). 1H NMR ($CDCl_3/300$ MHz) δ : 7.65-7.20 (m, 10H); 6.13-6.03 (m, 1H); 5.30-5.13 (m, 4H). Anal. Calcd for $C_{20}H_{15}BrF_3NO_2$: C, 54.81; H, 3.45; N, 3.20. Found: C, 54.69; H, 3.34; N, 3.19.

20

25 Example 28

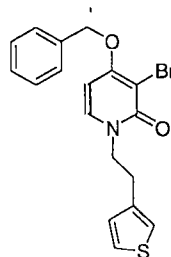
4-(benzyloxy)-3-bromo-1-(piperidin-3-ylmethyl)pyridin-
2(1H)-one hydrochloride



To the material of Example 11 (3.1 g, 0.011 mol) in DMF
5 (20 mL) was added dropwise sodium bis(trimethylsilyl)amide (1M
in THF, 12 mL). Contents were stirred one hour before adding
dropwise a solution of 3-methanesulfonyloxymethyl-1-
piperidine-1-carboxylic acid tert-butyl ester
(*Bioorg.Med.Chem.Lett*, 8(13), 1998, 1595-1600) (4.2 g, 0.015
10 mol) in DMF (5 mL). Contents were heated at 75°C overnight.
Contents were allowed to cool, poured into water (100 mL) and
a solid was filtered. The solid was stirred in 4 N
HCl/dioxane (15 mL) for 3 hours and filtered to give the
desired as a white solid, 752 mg (18% yield). mp 138.1-
15 139.2°C. FABHRMS m/z 377.0859 (M+H, C₁₈H₂₂BrN₂O₂ requires
377.0865). ¹H NMR (DMSO-d₆ /300 MHz): 9.50-9.10 (br, 2H);
8.00 (d, 1H); 7.50-7.30 (m, 5H); 6.93 (d, 1H); 5.30 (s, 2H);
4.30-3.90 (m, 3H); 3.40-3.10 (m, 3H); 2.80-2.50 (m, 3H); 2.40-
2.00 (m, 1H); 1.90-1.60 (m, 4H); 1.40-1.10 (m, 1H).
20 Anal. Calcd for C₁₈H₂₁BrN₂O₂ (2HCl, 0.25 H₂O): C, 47.55; H,
5.21; N, 6.16. Found: C, 47.48; H, 5.46; N, 6.27.

Example 29

4-(benzyloxy)-3-bromo-1-(2-thien-3-ylethyl)pyridin-2(1H)-
25 one

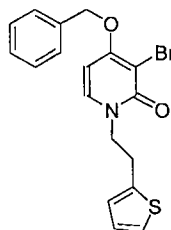


To the material of Example 11 (500 mg, 0.0018 mol) in DMF (5 mL) was added dropwise sodium bis(trimethylsilyl)amide (1M in THF, 2 mL). Contents were stirred one hour before adding
 5 dropwise a solution of methanesulfonic acid 2-thiophen-3-yl-ethyl ester (*J.A.C.S.*, 109(6), 1987, 1858-1859) (412 mg, 0.002 mol) in DMF (5 mL). Contents were heated at 75°C overnight. Contents were allowed to cool, poured into water (100 mL), and extracted into EtOAc, dried over MgSO₄, filtered, and
 10 concentrated in vacuo leaving a light yellow oil. The oil was purified by silica gel chromatography eluting with 50% EtOAc/hexanes to give the desired as a white solid, 199 mg (28% yield). mp 134.0-134.3°C.

FABHRMS m/z 390.0144 (M+H, C₁₈H₁₇BrNO₂S requires 390.0163). ¹H
 15 NMR (CDCl₃/300 MHz): 7.43-7.20 (m, 6H); 6.92-6.80 (m, 3H); 5.90 (d, 1H); 5.20 (s, 2H); 4.13 (t, 2H); 3.10 (t, 2H).
 Anal. Calcd for C₁₈H₁₆BrNO₂S: C, 55.39; H, 4.13; N, 3.59. Found: C, 55.21; H, 3.87; N, 3.52.

20 Example 30

4-(benzyloxy)-3-bromo-1-(2-thien-2-ylethyl)pyridin-2(1H)-one



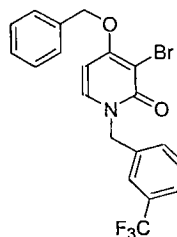
The title compound was prepared essentially according to
 25 the procedure of Example 29. mp 128.0-129.5°C. FABHRMS m/z

390.0160 (M+H, $C_{18}H_{17}BrNO_2S$ requires 390.0163). 1H NMR (CDCl₃/300 MHz) δ : 7.48-7.30 (m, 5H); 7.12 (d, 1H); 6.95-6.80 (m, 2H); 6.75-6.68 (m 1H); 5.95 (d, 1H); 5.20 (s, 2H); 4.16 (t, 2H); 3.30 (t, 2H).

5 Anal. Calcd for $C_{18}H_{16}BrNO_2S$: C, 55.39; H, 4.13; N, 3.59. Found: C, 55.06; H, 4.01; N, 3.56.

Example 31

4-(benzyloxy)-3-bromo-1-[3-(trifluoromethyl)
10 benzyllpyridin-2(1H)-one

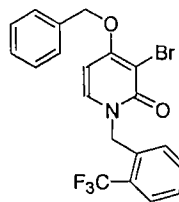


To the material of Example 11 (500 mg, 0.0018 mol) in DMF (5 mL) was added dropwise sodium bis(trimethylsilyl)amide (1M
15 in THF, 2 mL). Contents were stirred one hour before adding dropwise a solution of 3-trifluoromethylbenzyl bromide (478 mg, 0.002 mol) in DMF (5 mL). Contents were heated at 75°C for 2 hours. Contents were allowed to cool, poured into water (100 mL), and extracted with EtOAc, which was dried over MgSO₄,
20 filtered, and concentrated *in vacuo* leaving a white solid. FABHRMS *m/z* 438.0301 (M+H, $C_{20}H_{16}BrF_3NO_2$ requires 438.0316). 1H NMR (CDCl₃/300 MHz): 7.60-7.20 (m, 10H); 6.10 (d, 1H); 5.14 (s, 2H); 5.20 (s, 2H).

Anal. Calcd for $C_{20}H_{15}BrF_3NO_2$: C, 54.81; H, 3.45; N, 3.20.
25 Found: C, 54.81; H, 3.36; N, 3.13.

Example 32

4-(benzyloxy)-3-bromo-1-[2-(trifluoromethyl)
benzyllpyridin-2(1H)-one



The material of Example 32 was prepared according to the procedure of Example 31.

FABHRMS m/z 438.0280 ($M+H$, $C_{20}H_{16}BrF_3NO_2$ requires 438.0316). 1H

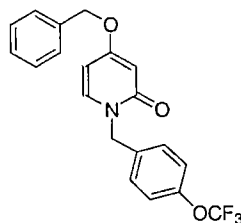
5 NMR ($CDCl_3$ /300 MHz) δ : 7.68 (d, 1H); 7.55-7.20 (m, 8H); 7.15 (d, 1H); 6.10 (d, 1H); 5.40 (s, 2H); 5.13 (s, 2H).

Anal. Calcd for $C_{20}H_{15}BrF_3NO_2$: C, 54.81; H, 3.45; N, 3.20.

Found: C, 54.48; H, 3.36; N, 3.17.

10 Example 33

4-(benzyloxy)-1-[4-(trifluoromethoxy)benzyl]pyridin-2(1H)-one



15 The material of Example 33 was prepared according to the procedure of Example 1.

FABHRMS m/z 376.1158 ($M+H$, $C_{20}H_{17}F_3NO_3$ requires 376.1161). 1H

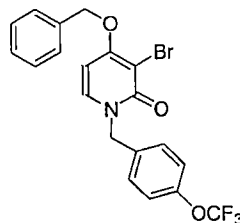
NMR ($CDCl_3$ /300 MHz) δ : 7.40-7.05 (m, 10H); 6.05-5.95 (m, 2H); 5.06 (s, 2H); 4.98 (s, 2H).

Anal. Calcd for $C_{20}H_{16}F_3NO_3$: C, 64.00; H, 4.30; N, 3.73.

20 Found: C, 63.97; H, 4.26; N, 3.57.

Example 34

4-(benzyloxy)-3-bromo-1-[4-(trifluoromethoxy)benzyl]pyridin-2(1H)-one



The material of Example 34 was prepared according to the procedure of Example 2.

FABHRMS m/z 454.0240 ($M+H$, $C_{20}H_{16}BrF_3NO_3$ requires 454.0266). 1H

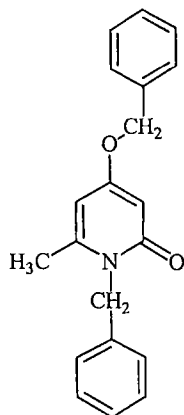
5 NMR ($CDCl_3$ /300 MHz) δ : 7.45-7.10 (m, 10H); 6.08 (d, 1H); 5.20 (s, 2H); 5.12 (s, 2H).

Anal. Calcd for $C_{20}H_{15}BrF_3NO_3$: C, 52.88; H, 3.33; N, 3.08.

Found: C, 52.53; H, 3.09; N, 2.92.

10 Example 35

1-benzyl-4-(benzyloxy)-6-methylpyridin-2(1H)-one



Step 1: Preparation of 1-benzyl-4-hydroxy-6-methylpyridin-2(1H)-one.

4-hydroxy-6-methyl-2-pyrone (0.2 mol, 25.2 g) and benzylamine (0.2 mol, 21.4 g) were added to water (800 mL) and heated to reflux with stirring for 2 hours. After cooling to room temperature, a light brown solid was collected by
 20 filtration. (33.4 g, 77%): 1H NMR ($DMSO-d_6$ /300 MHz) δ : 10.5 (s, 1H), 7.4-7.1 (m, 5 H), 5.8-5.6 (m, 2H), 5.2 (s, 2H), 5.1

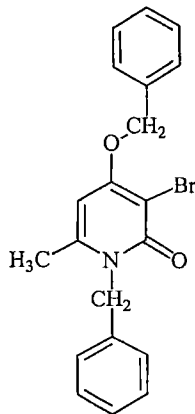
(s, 2H), 2.2 (s, 3H). ESHRMS m/z 216.100 (M+H, $C_{12}H_{13}NO_2$ requires 216.102).

Step 2: Preparation of 1-benzyl-4-(benzyloxy)-6-methylpyridin-2(1H)-one.

1-benzyl-4-hydroxy-6-methylpyridin-2(1H)-one (10 mmol, 2.15 g), dichloromethane (100 mL), benzylbromide (11 mmol, 1.88 g), sodium hydroxide (2.5 N, 20 mmol, 8 mL), and benzyltriethylammonium chloride (0.5 g) were vigorously stirred at room temperature for 16h. Hydrochloric acid (1 N) was added until the mixture produced an acidic reaction to pH paper. The mixture was then extracted with ethyl acetate (3 X 50 mL). The combined organic extracts were washed with brine, dried over magnesium sulfate, filtered, and concentrated. The product was obtained by flash chromatography eluting with ethyl acetate : hexanes (1:2). The appropriate fractions were concentrated to a clear oil. (1.3 g, 43%): 1H NMR (DMSO- d_6 /300 MHz) δ : 7.4-7.1 (m, 10 H), 6.0-5.9 (m, 2H), 5.2 (s, 2H), 5.1 (s, 2H), 2.2 (s, 3H). ESHRMS m/z 306.147 (M+H, $C_{20}H_{19}NO_2$ requires 306.149).

Example 36

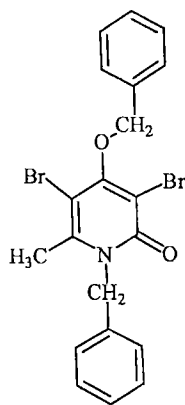
1-benzyl-4-(benzyloxy)-3-bromo-6-methylpyridin-2(1H)-one



The product from example 35, 1-benzyl-4-(benzyloxy)-6-methylpyridin-2(1H)-one (4.2 mmol, 1.3 g), acetic acid (50 mL), and sodium acetate (5.0 mmol, 0.41 g) were stirred at room temperature. Bromine (4.2 mmol, 0.67 g) was added drop wise with stirring. After ½ hour, water (100 mL) was added and the mixture was extracted with ethyl acetate (3 X 50 mL). The combined organic extracts were washed with saturated aqueous sodium bicarbonate solution and brine. After drying over magnesium sulfate and concentrating, the mixture was purified by flash column chromatography eluting with ethyl acetate : hexanes (1 : 2). The appropriate fractions were concentrated to yield a light oil. (1.0 g, 62%): ¹H NMR (DMSO-d₆/300 MHz) 7.4-7.0 (m, 10 H), 6.5 (s, 1H), 5.29 (s, 2H), 5.27 (s, 2H), 2.2 (s, 3H). ESHRMS *m/z* 384.057 (M+H, C₂₀H₁₈NO₂Br requires 384.060).

Example 37

1-benzyl-4-(benzyloxy)-3,5-dibromo-6-methylpyridin-2(1H)-one



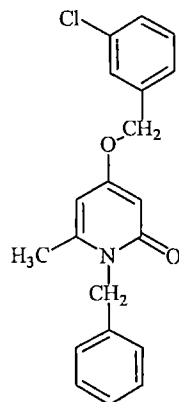
20

The product from example 35, 1-benzyl-4-(benzyloxy)-6-methylpyridin-2(1H)-one (4.2 mmol, 1.3 g), acetic acid (50 mL), and sodium acetate (5.0 mmol, 0.41 g) were stirred at room temperature. Bromine (4.2 mmol, 0.67 g) was added drop wise with stirring. After ½ hour, water (100 mL) was added and the mixture was extracted with ethyl acetate (3 X 50 mL).

The combined organics were washed with saturated aqueous sodium bicarbonate solution and brine. After drying over magnesium sulfate and concentrating, the mixture was purified by flash column chromatography eluting with ethyl acetate :
5 hexanes (1 : 2). The appropriate fractions were concentrated to yield a white solid. (0.3 g, 15%): ^1H NMR (DMSO- d_6 /300 MHz) 7.5-7.0 (m, 10 H), 5.42 (s, 2H), 5.07 (s, 2H), 2.45 (s, 3H). ESHRMS m/z 463.966 (M+H, $\text{C}_{20}\text{H}_{17}\text{NO}_2\text{Br}_2$ requires 463.968).

10 Example 38

1-benzyl-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one



15 Step 1: Preparation of 1-benzyl-6-methyl-2-oxo-1,2-dihydropyridin-4-yl 4-bromobenzenesulfonate.

1-benzyl-4-hydroxy-6-methylpyridin-2(1H)-one (from example 35) (10 mmol, 2.15 g), N,N'-dimethylformamide (30 mL), potassium carbonate (20 mmol, 2.76 g), and 4-bromobenzenesulfonyl chloride (10 mmol, 2.55 g) were stirred
20 at room temperature for 16 hours. Hydrochloric acid (1N) was added until the mixture was acidic to pH paper. Brine (50 mL) was added and the mixture extracted with ethyl acetate (3 X 50 mL). The combined organic extracts were washed with brine and
25 dried over magnesium sulfate, and filtered. After concentrating, the material was purified by flash column

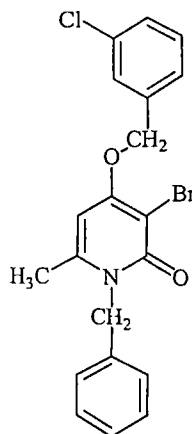
chromatography eluting with ethyl acetate:hexanes (1:2). The appropriate fractions were concentrated to a clear oil, which solidified upon standing several days to a white solid. (3.3 g, 76%): ^1H NMR (DMSO- d_6 /400 MHz) 7.9 (m, 4H), 7.32-7.00 (m, 5H), 7.3 (m, 1H), 6.12 (d, $J = 2.4$ Hz, 1H), 6.02 (d, $J = 2.8$ Hz, 1H), 5.20 (s, 2H), 2.2 (s, 3H). ESHRMS m/z 436.002 (M+H, $\text{C}_{19}\text{H}_{16}\text{NO}_4\text{SBr}$ requires 436.004).

Step 2: Preparation of 1-benzyl-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one.

1-benzyl-6-methyl-2-oxo-1,2-dihydropyridin-4-yl 4-bromobenzenesulfonate (3.0 mmol, 1.3 g), N,N' -dimethylformamide (30 mL), 3-chlorobenzyl alcohol (3.0 mmol, 0.43 g), and sodium hydroxide (60%, 3.3 mmol, 0.13 g) were stirred at room temperature under nitrogen for 4 hours. Hydrochloric acid (1 N, 10 mL) was added and the mixture extracted with ethyl acetate (3 X 25 mL). The combined organic extracts were washed with saturated aqueous sodium bicarbonate solution and brine. After drying over magnesium sulfate and concentrating, the mixture was purified by flash column chromatography eluting with ethyl acetate:hexanes (1:1) to obtain a light yellow oil. (14.3 g, 64%): ^1H NMR (DMSO- d_6 /300 MHz) δ : 7.4-7.0 (m, 10 H), 6.0-5.8 (m, 2H), 5.2 (s, 2H), 5.0 (s, 2H), 2.1 (s, 3H). ESHRMS m/z 340.110 (M+H, $\text{C}_{20}\text{H}_{18}\text{NO}_2\text{Cl}$ requires 340.110).

Example 39

1-benzyl-3-bromo-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one

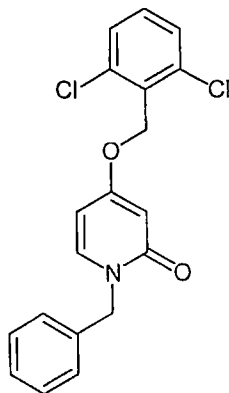


The product of example 38 (SC-83316), 1-benzyl-4-[(3-chlorobenzyl)oxy]-6-methylpyridin-2(1H)-one (0.91 mmol, 310 Mg), acetic acid (20 mL), and sodium acetate (0.91 mmol, 80
 5 Mg) were stirred at room temperature when bromine (0.91 mmol, 145 Mg) was added. After stirring for one hour, the mixture was concentrated, dissolved in ethyl acetate, and washed successively with saturated aqueous sodium bicarbonate solution, brine, and water. After drying over magnesium
 10 sulfate and concentrating, the product was recrystallized from tetrahydrofuran / hexanes to yield a white solid. (240 Mg, 63%): ¹H NMR (DMSO-d₆/300 MHz) 7.6-7.0 (m, 10 H), 6.5 (s, 1H), 5.33 (s, 2H), 5.33 (s, 2H), 2.3 (s, 3H). ESHRMS m/z 420.019 (M+H, C₂₀H₁₇NO₂BrCl requires 420.019).

15

EXAMPLE 40

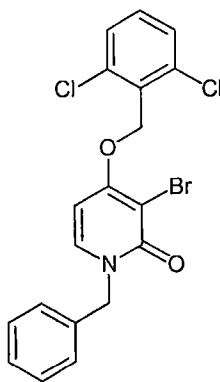
1-Benzyl-4-[2,6-(dichlorobenzyl)oxy]pyridin-2(1H)-one



The title compound was prepared essentially as described in claim 1. mp 151.6-152.0 °C. ¹H NMR (CDCl₃/300MHz) δ: 7.31 (m, 8H), 7.12 (d, 1H, J = 7.45 Hz), 6.13 (d, 1H, J = 2.42 Hz), 5.90 (dd, 1H, J = 2.62 Hz), 5.22 (s, 2H), 5.10 (s, 2H).
5 ESHRMS m/z 360.0551 (M+H C₁₉H₁₅Cl₂NO₂ requires 360.0558).

EXAMPLE 41

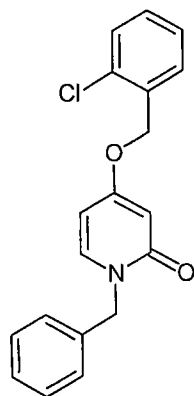
1-Benzyl-3-bromo-4-[2,6-(dichlorobenzyl)oxy]pyridin-2(1H)-one



1-Benzyl-4-[2,6-(dichlorobenzyl)oxy]pyridin-2(1H)-one (0.400 g, 1.11 mmol) was dissolved in acetic acid (10 mL). Sodium acetate (0.091 g, 1.11 mmol) was added, and the mixture was cooled to 15 °C. Bromine (0.195 g, 1.22 mmol) was added
15 via syringe. The reaction stirred at room temperature for 2 hours. Water (15 mL) was added, and the mixture transferred to a separatory funnel. Ethyl acetate (50 mL) was added and the layers were separated. The organic phase was washed with aqueous NaHCO₃ (2 x 25 mL), dried over MgSO₄, filtered, and
20 evaporated to yield a white solid. ¹HNMR (CDCl₃/300MHz) δ: 7.34 (m, 9H), 6.24 (d, 1H, J = 7.65 Hz), 5.37 (s, 2H), 5.18 (s, 2H). ESHRMS m/z 439.9646 (M+H C₁₉H₁₄BrCl₂NO₂ requires 439.9641).

25 Example 42

1-Benzyl-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one



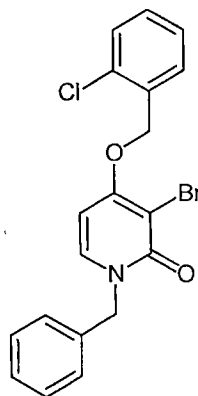
The title compound was prepared by a procedure similar to the one described in Example 1. mp 124.6-125.0 °C. ¹HNMR (CDCl₃/300MHz) δ: 7.36 (m, 9H), 7.14 (d, 1H, J = 7.65 Hz), 6.04 (d, 1H, J = 2.62 Hz), 5.98 (d, 1H, J = 2.82 Hz), 5.10 (s, 2H), 5.09 (s, 2H). ESHRMS m/z 326.0950 (M+H C₁₉H₁₆ClNO₂ requires 326.0948).

Anal. Calc'd. for C₁₉H₁₆ClNO₂: C, 70.05; H, 4.95; N, 4.30; Cl, 10.88. Found: C, 69.87; H, 4.74; N, 4.42, Cl, 11.08.

10

EXAMPLE 43

1-Benzyl-3-bromo-4-[(2-chlorobenzyl)oxy]pyridin-2(1H)-one

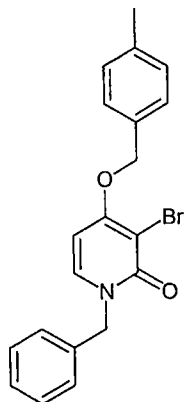


The title compound was prepared by a procedure similar to the one described in Example 2. mp 143.3-145.5 °C. ¹HNMR (CDCl₃/300MHz) δ: 7.63 (d, 2H, J = 1.81 Hz), 7.44 (m, 9H), 6.06 (d, 1H, J = 7.65 Hz), 5.29 (s, 2H), 5.17 (s, 2H). ESHRMS m/z 406.0036 (M+H C₁₉H₁₅BrClNO₂ requires 406.0032).

Anal. Calc'd. for $C_{19}H_{15}Cl\ BrNO_2$: C, 56.39; H, 3.74; N, 3.46; Cl, 8.76. Found: C, 56.01; H, 3.38; N, 3.36, Cl, 9.01.

EXAMPLE 44

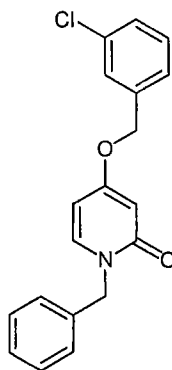
5 1-Benzyl-3-bromo-4-[(4-methylbenzyl)oxy]pyridin-2(1H)-one



The title compound was prepared by a procedure similar to the one described in Example 2. mp 149.0-149.7 °C. 1H NMR (CDCl₃/300MHz) δ : 7.25 (m, 10H), 6.04 (d, 1H, J = 7.65 Hz), 5.17 (s, 2H), 5.15 (s, 2H), 2.34 (s, 3H). ESHRMS m/z 386.0583 (M+H C₂₀H₁₈BrNO₂ requires 386.0581).

EXAMPLE 45

1-Benzyl-4-[(3-chlorobenzyl)oxy]pyridin-2(1H)-one

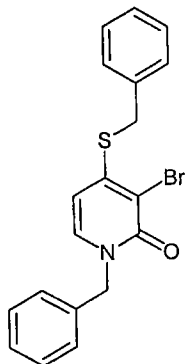


15 The title compound was prepared by a procedure similar to the one described in Example 1. mp 95.5-95.7 °C. 1H NMR (CDCl₃/300MHz) δ : 7.34 (m, 9H), 7.13 (d, 1H, J = 7.45 Hz), 5.96

(m, 1H), 5.95 (d, 1H, $J = 7.45$ Hz), 5.09 (s, 2H), 4.96 (s, 2H).. ESHRMS m/z 326.0977 ($M+H$ $C_{19}H_{16}ClNO_2$ requires 326.0948).

EXAMPLE 46

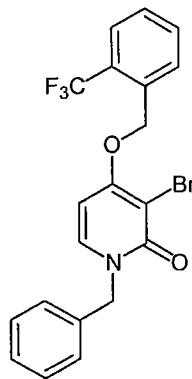
5 1-Benzyl-4-[benzylthio]-3-bromopyridin-2(1H)-one



The title compound was prepared by a procedure similar to the one described in Example 2. mp 180.6-182.1 °C. 1H NMR ($CDCl_3/300MHz$) δ : 7.33 (m, 10H), 7.14 (d, 1H, $J = 7.45$ Hz), 6.08 (d, 1H, $J = 7.45$ Hz), 5.13 (s, 2H), 4.15 (s, 2H). ESHRMS m/z 386.0211 ($M+H$ $C_{19}H_{16}BrNOS$ requires 386.0214).

EXAMPLE 47

1-Benzyl-3-bromo-4-{ [2-(trifluoromethyl)benzyl]oxy}pyridin-2(1H)-one

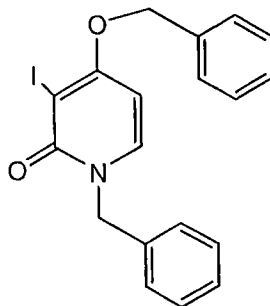


The title compound was prepared by a procedure similar to the one described in Example 2. mp 133.2-133.5 °C. 1H NMR ($CDCl_3 / 300MHz$) δ : 7.81 (d, 1H, $J = 7.65$ Hz), 7.68 (d, 1H, $J = 7.65$ Hz), 7.61 (t, 1H, $J = 7.65$ Hz), 7.38 (m, 7H), 6.01 (d,

1H, J = 7.85 Hz), 5.39 (s, 2H), 5.16 (s, 2H). ESHRMS m/z 438.0313 (M+H C₂₀H₁₅BrF₃NO₂ requires 403.0316).

Example 48

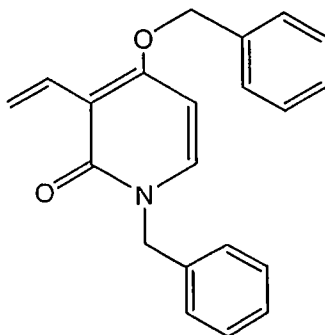
5 1-benzyl-4-(benzyloxy)-3-iodopyridin-2(1H)-one



A mixture of N,O-dibenzyl-2-pyridone (2.0 g, 6.87 mmol), N-iodosuccinimide (1.7 g), dichloroacetic acid (0.15 mL) in acetonitrile (40.0 mL) was heated at 65 °C under argon
10 atmosphere for 3.5 h, with constant stirring. The reaction mixture was concentrated to dryness, and the residue was purified by silica gel flash chromatography using EtOAc/hexanes 1:1 v/v to give the title compound 2.3 g (80%) as a flaky white solid: ¹H-NMR (CDCl₃) δ: 7.4 - 7.2 (m, 10 H), 7.19
15 (1H, d, J = 7.6 Hz), 5.95 (d, 1H, J = 7.6 Hz), 5.2 (s, 1H), 5.15 (s, 2H); ER-MS m/z = 418 (MH⁺); HR-MS m/z calcd C₁₉H₁₇NO₂ 418.0304, found 418.0277.

Example 49

20 1-benzyl-4-(benzyloxy)-3-vinylpyridin-2(1H)-one

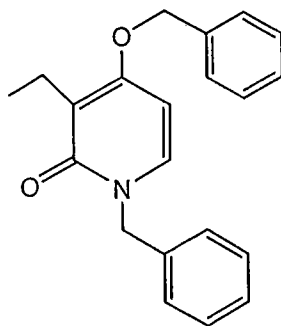


A solution of 1-benzyl-4-(benzyloxy)-3-iodopyridin-2(1H)-one (1.9 g, 4.56 mmol) and vinyl-tri-butyltin (2.5 mL) in acetonitrile (20.0 mL) containing DMF (2.0 mL) was degassed using house vacuum and purged with argon. Then added
5 PdCl₂(PPh₃)₂ (0.3 g) and the mixture was heated at 65 °C under argon atmosphere for 4 h, with stirring. The solvents were distilled in vacuo, and the residue was triturated with EtOAc and filtered through a pad of celite. The filtrate was concentrated and the residue was purified by silica gel flash chromatography using 25% EtOAc in hexanes to give the title
10 compound (0.75 g, 50%) as an orange colored solid.

¹H-NMR (CDCl₃) δ: 7.4 - 7.2 (m, 10 H), 7.14 (d, 1H, J = 7.6 Hz), 7.05 (dd, 1H, J = 12.0 Hz), 6.47 (dd, 1H, J = 2.8 Hz), 6.07 (d, 1H, J = 7.6 Hz), 5.4 (dd, 1H, J = 2.8 Hz), 5.13
15 (s, 4H); ER-MS m/z = 418 (MH⁺); ER-MS m/z = 318 (MH⁺); HR-MS m/z calcd C₂₁H₂₀NO₂ 318.1494, found 318.1480.

Example 50

1-benzyl-4-(benzyloxy)-3-ethylpyridin-2(1H)-one



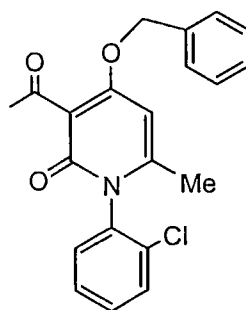
20

To a solution of 1-benzyl-4-(benzyloxy)-3-vinylpyridin-2(1H)-one (0.5 g, 1.6 mmol) in EtOH (10.0 mL) and EtOAc (10.0 mL) was added Pd/C (10 %, 0.25 g) and stirred in an atmosphere of hydrogen gas at 30 psi for 16 h. The catalyst was removed
25 by filtration, the filtrate was concentrated to dryness and the resulting residue was purified by silica gel flash chromatography using EtOAc/hexanes (1:1, v/v) to afford the

title compound (0.32 g, 64%) as a pale yellow powder: $^1\text{H-NMR}$ (CD_3OD) δ : 7.52 (d, 1H, $J = 7.6$ Hz), 7.39 - 7.2 (m, 10 H), 6.41 (d, 1H, $J = 7.6$ Hz), 5.18 (s, 2H), 5.15 (s, 2H), 2.58 (q, 2H, $J = 7.2$ Hz), 1.03 (t, 3H, $J = 7.2$ Hz), ER-MS $m/z = 320$ (MH^+);
 5 HR-MS m/z calcd $\text{C}_{21}\text{H}_{22}\text{NO}_2$ 320.1651, found 320.1648.

Example 51

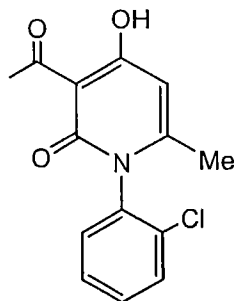
3-acetyl-4-(benzyloxy)-1-(2-chlorophenyl)-6-methylpyridin-2(1H)-one



10

Step A

Preparation of 3-acetyl-1-(2-chlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-one



15 A mixture of 2-chlorophenylisocyanate (3.0 g, 19.53 mmol), and diketene (3.3 g, 39.28 mmol) in toluene (10.0 mL) containing triethylamine (0.05 mL) was heated to reflux for 6 h, under an atmosphere of argon. Toluene was distilled in vacuo and the resulting residue was purified by silica gel
 20 flash chromatography using 25 % EtOAc in hexanes as the eluent to afford the title compound (0.85 g, see ref: *Heterocycles* 27 (9), 2063, 1988.) as a pale yellow solid: $^1\text{H-NMR}$ (CD_3OD) δ :

7.63 (m, 1H), 7.52 (m, 2H), 7.4 (m, 1H), 6.14 (s, 1H), 2.58 (s, 3H), and 1.95 (s, 3H); ES-MS m/z = 278 (MH^+).

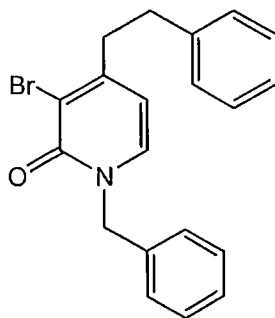
Step B

5 Preparation of 3-acetyl-4-(benzyloxy)-1-(2-chlorophenyl)-6-methylpyridin-2(1H)-one

To a solution of 3-acetyl-1-(2-chlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-one (0.56 g, 2.02 mmol) in DMF (5.0 mL), benzyl bromide (0.3 mL) and potassium carbonate (0.3 g, 2.16 mmol) were added. The mixture was stirred at room temperature for 3 h, and at 65 °C for 1 h under argon atmosphere. The reaction mixture was concentrated in vacuo and the residue was partitioned between 5% citric acid (25 mL) and EtOAc (50.0 mL). The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The resulting residue was purified by silica gel flash chromatography using 50% EtOAc in hexanes to afford the title compound (0.58 g, 75%) as a pale yellow amorphous substance: 1H -NMR (CD_3OD) δ : 7.65 – 7.3 (m, 9H), 6.5 (s, 1H), 5.31 (s, 2H), 2.42 (s, 3H), and 2.01 (s, 3H); ER-MS m/z = 368 (MH^+); HR-MS m/z calcd $C_{21}H_{19}NO_3Cl$, 368.1060, found 368.1053.

Example 52

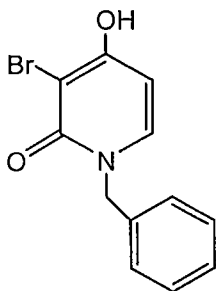
1-benzyl-3-bromo-4-(2-phenylethyl)pyridin-2(1H)-one



25

Step A

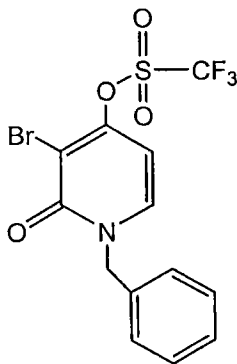
Preparation of 1-benzyl-3-bromo-4-hydroxypyridin-2(1H)-
one



A suspension of N-benzyl-4-hydroxy-2-pyridone (0.75 g,
5 3.7 mmol), NBS (0.7 g, 1.05 mmol) in dichloromethane was
stirred at room temperature for 1.5 h under argon atmosphere.
It was diluted with dichloromethane (25 mL), cooled and
filtered. The solids were washed with dichloromethane and
dried in vacuo. The filtrate and the washings were combined
10 and washed with water, dried (Na_2SO_4), filtered, and
concentrated to dryness. The resulting residue was washed
with EtOAc, and dried in vacuo to give a combined mass of 0.65
g of the title compound as a white powder: ^1H NMR (CD_3OD) δ :
7.54 (d, 1H, $J = 7.6$ Hz), 7.27 (m, 5H), 6.12 (d, 1H, $J = 7.6$
15 Hz), 5.15 (s, 2H); ES-MS: $m/z = 280$ (MH^+).

Step B

Preparation of 1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-
4-yl trifluoromethanesulfonate

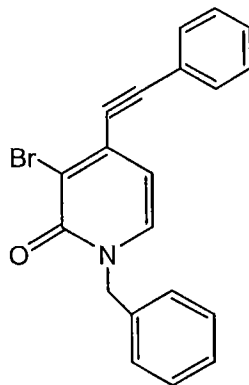


To a cold (-30 °C) suspension of 1-benzyl-3-bromo-4-hydroxypyridin-2(1H)-one (0.78 g, 2.8 mmol) in dichloromethane (10.0 mL), was added triethylamine (0.6 mL, 4.28 mmol), followed by the addition of triflic anhydride (0.7 mL, 4.17 mmol). The resulting mixture was stirred at -30 °C under argon atmosphere for 1 h. The reaction mixture was then poured into ice/water mixture (50 mL) and the products were extracted with dichloromethane (2 x 25 mL). The combined organic extracts were washed with water (2 x 20 mL), dried (Na₂SO₄), filtered, and concentrated to dryness. The residue was dried in vacuo to afford the desired trifluorosulfonate (1.0 g) as a pale yellow solid which used as such in the next step: ¹H- NMR (CDCl₃) δ: 7.35 (m, 6H), 6.26 (d, 1H, J = 8.0 Hz); ¹⁹F- NMR (CDCl₃) δ: -73.73 ppm; ES-MS: m/z = 412 (MH⁺).

15

Step C

Preparation of 1-benzyl-3-bromo-4-(phenylethynyl)pyridin-2(1H)-one.



To a solution of 1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-4-yl trifluoromethanesulfonate (1.0 g) in DMF (5.0 mL) was added phenylacetylene (0.4 mL) and degassed using house vacuum. The reaction flask was then purged with argon, added diisopropylethylamine (0.53 mL), and PdCl₂(PPh₃)₂ (0.35 g) were added. The resulting mixture was stirred at room temperature for 15 min and heated at 65 °C under an argon

25

atmosphere for 3h. The dark colored reaction mixture was concentrated in vacuo, and the residue was partitioned between EtOAc (50 mL) and 5% aqueous citric acid (25 mL). The organic extracts were washed with water, dried (Na_2SO_4), filtered, and concentrated to dryness. The resulting material was purified by silica gel flash chromatography using 25% EtOAc in hexanes as the eluent. The appropriate fractions were combined, concentrated under reduced pressure. ^1H NMR (CDCl_3) δ : 7.57 (m, 2H), 7.38 (m, 8H), 7.21 (d, 1H, $J = 6.8$ Hz), 6.25 (d, 1H, $J = 6.8$ Hz), and 5.16 (d, 2H), ES-MS: $m/z = 364$ (MH^+); HR-MS m/z (MH^+) calcd $\text{C}_{20}\text{H}_{15}\text{NOBr}$ 364.0337, found 364.0337.

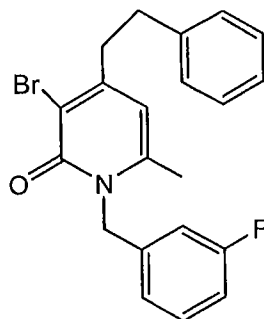
Step D

Preparation of 1-benzyl-3-bromo-4-(2-phenylethyl)pyridin-2(1H)-one.

A mixture of 1-benzyl-3-bromo-4-(phenylethynyl)pyridin-2(1H)-one (0.3 g), and platinum oxide (0.05 g) in a solvent mixture of EtOAc (10.0 mL) and EtOH (10.0 mL) was stirred in an atmosphere of hydrogen at 15 psi in a Fischer porter bottle for 45 min. The catalyst was removed by filtration, and filtrate was concentrated. The resulting residue was purified by silica gel flash chromatography using 25% EtOAc in hexanes as the eluent. The appropriate fractions (visualized under an UV lamp) were combined and concentrated under reduced pressure. ^1H -NMR (CD_3OD) δ : 7.56 (d, 1H, $J = 6.8$ Hz), 7.31 - 7.17 (m, 10 H), 6.24 (d, 1H, $J = 6.8$ Hz), 5.19 (s, 2H), 2.96 (m, 2H), and 2.91 (m, 2H); ES-MS $m/z = 368$ (MH^+); HR-MS m/z (MH^+) calcd $\text{C}_{20}\text{H}_{19}\text{NOBr}$ 368.0650, found 368.0630.

Example 53

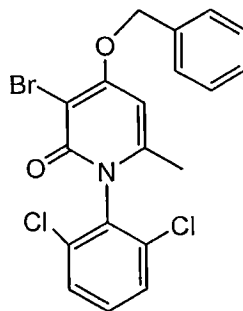
3-bromo-1-(3-fluorobenzyl)-6-methyl-4-(2-phenylethyl)pyridin-2(1H)-one



The title compound was prepared essentially according to the procedure of Example 52. ^1H -NMR δ : (CD_3OD) δ : 7.35 (m, 1H), 7.31–7.16 (m, 5H), 6.99 (m, 1H), 6.91 (m, 1H), 6.81 (m, 1H), 6.20 (s, 1H), 5.41 (s, 2H), 2.94 (m, 4H), and 2.24 (s, 3H); ^{19}F -NMR (CD_3OD) δ : -115.01 (m); ES-MS, m/z = 400 (MH^+); HR-MS m/z calcd $\text{C}_{21}\text{H}_{20}\text{NOBrF}$ 400.0712, found 400.0695.

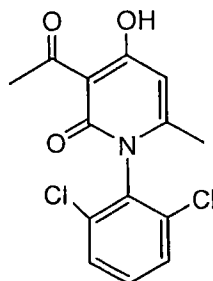
10 Example 54

4-(benzyloxy)-3-bromo-1-(2,6-dichlorophenyl)-6-methylpyridin-2(1H)-one



Step A

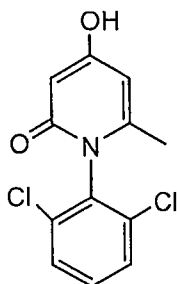
15 Preparation of 3-acetyl-1-(2,6-dichlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-one



A mixture of 2,6 dichlorophenylisocyanate (4.8 g, 0.025 mol), and diketene (4.3 g, 0.05 mol) in toluene (15.0 mL) was heated to reflux for 4 h under an atmosphere of argon. After removal of the solvent in vacuo, the residue was purified by silica gel flash chromatography using EtOAc/hexanes (1:3 v/v). The appropriate fractions, as monitored by ES mass spectrometry ($MH^+ m/z = 312$) were combined and concentrated under reduced pressure. The resulting yellow solid (2.3 g) was further purified by reverse-phase HPLC using 10-90% acetonitrile/water gradient (45 min) at a flow rate of 100 mL/min. The appropriate fractions, as monitored by ES mass spectrometry ($MH^+ m/z = 312$) were combined and concentrated to half the volume. The solid that separated was extracted with EtOAc (2 x 25 mL). The combined extracts were washed with water, dried (Na_2SO_4), filtered, and concentrated to dryness to give the title compound (0.77 g) as a pale yellow powder: 1H -NMR (CD_3OD) δ : 7.62 (m, 2H), 7.52 (m, 1H), 6.19 (s, 1H), 2.59 (s, 3H), and 1.96 (s, 3H); ES-MS $m/z = 312$ (MH^+); HR-MS, m/z calc $C_{14}H_{12}NO_3Cl_2$ 312.0189, found 312.0214.

Step B.

Preparation of 1-(2,6-dichlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-one



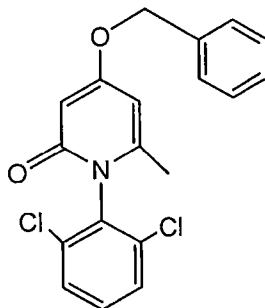
A mixture of 3-acetyl-1-(2,6-dichlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-one 0.7 g (0.002mol) in n-butanol (3.0 mL) containing sulfuric acid (1.5 mL) was heated at 120 °C for 4 h. The dark reaction mixture was cooled, added ice/water (25

mL), and extracted with EtOAc (2 x 25 mL). The combined organic extracts were washed with water, dried (Na_2SO_4), filtered, concentrated under reduced pressure and the resulting material was purified by silica gel flash chromatography using 25% EtOAc in hexanes as the eluent to afford the title compound (0.14 g) as a pale yellow powder: ^1H -NMR (CD_3OD) δ : 7.6 (m, 2H), 7.48 (m, 1H), 6.10 (dd, 1H), 5.78 (d, 1H, $J = 2.4$ Hz), 1.91 (s, 3H); ES-MS $m/z = 270$ (MH^+); HR-MS, m/z calc $\text{C}_{12}\text{H}_{10}\text{NO}_2\text{Cl}_2$ 270.0083, found 270.0103.

10

Step C

Preparation of 4-(benzyloxy)-1-(2,6-dichlorophenyl)-6-methylpyridin-2(1H)-one



15 A mixture of 1-(2,6-dichlorophenyl)-4-hydroxy-6-methylpyridin-2(1H)-one (0.125 g, 0.46 mmol) and benzylbromide (0.1 mL) in DMF (2.5 mL) was stirred at room temperature for 16 h. The reaction mixture was diluted with water (10.0 mL) and extracted with EtOAc (2 x 20 mL). The
20 combined organic extracts were washed with water, dried (Na_2SO_4), filtered, concentrated under reduced pressure and the resulting material was purified by silica gel flash chromatography using 25% EtOAc in hexanes to afford the title compound (0.11 g) as a pale yellow syrup: ^1H -NMR (CD_3OD) δ :
25 7.61 (m, 2H), 7.55-7.3 (m, 6H), 6.23 (d, 1H, $J = 2.0$ Hz), 6.01 (d, 1H, $J = 2.0$ Hz), 5.12 (s, 2H), and 1.93 (s, 3H); ES-MS

m/z=360 (MH^+); HR-MS, m/z calc $\text{C}_{19}\text{H}_{16}\text{NO}_2\text{Cl}_2$, 360.0553, found 360.0569.

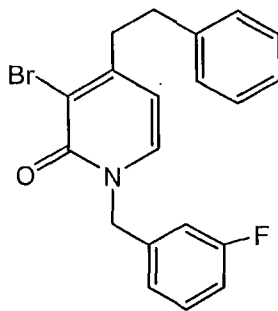
Step D

5 Preparation of 4-(benzyloxy)-3-bromo-1-(2,6-dichlorophenyl)-6-methylpyridin-2(1H)-one

A mixture of 4-(benzyloxy)-1-(2,6-dichlorophenyl)-6-methylpyridin-2(1H)-one (0.1 g, 0.278 mmol) and N-bromosuccinimide (0.055 g, 0.3 mmol) in dichloroethane (3.0 mL) was stirred at room temperature for 1 h, and heated at 60 °C under argon for 30 min. The reaction mixture was then diluted with dichloroethane (15 mL), washed with water, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. ^1H NMR (CD_3OD) δ : 7.64 (m, 2H), 7.55 (m, 3H), 7.38 (m, 3H), 6.65 (s, 1H), 5.34 (s, 2H), and 2.00 (s, 3H); ES-MS m/z = 439 (MH^+); HR-MS, m/z calc $\text{C}_{19}\text{H}_{16}\text{NO}_2\text{Cl}_2\text{Br}$, 439.9635, found 439.9669.

Example 55

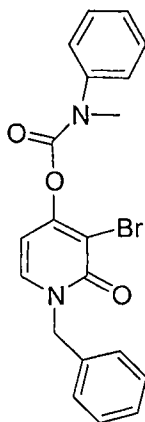
3-bromo-1-(3-fluorobenzyl)-4-(2-phenylethyl)pyridin-2(1H)-one



The title compound was prepared essentially according to the procedure of Example 52. ^1H -NMR (CD_3OD) δ : 7.58 (d, 1H, J = 6.8 Hz), 7.4-7.0 (m, 9H), 6.26 (d, 1H, J = 6.8 Hz), 5.19 (s, 2H), 2.97 (m, 2H), and 2.90 (m, 2H); ES-MS m/z = 386 (MH^+); HR-MS, m/z calc $\text{C}_{20}\text{H}_{18}\text{NOFBr}$, 386.0550, found 386.0585.

Example 56

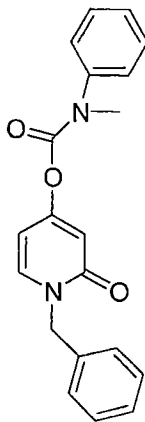
1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-4-yl
methyl (phenyl) carbamate



5

Step A

Preparation of 1-benzyl-2-oxo-1,2-dihydropyridin-4-yl
methyl (phenyl) carbamate



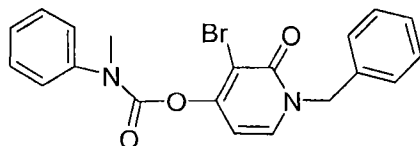
10 To a chilled solution of 1-benzyl-4-hydroxypyridin-2(1H)-
one (0.375 g, 1.86 mmol) in anhydrous acetonitrile (10 mL) was
added triethylamine (0.206 g, 2.04 mmol) followed by N-methyl-
N-phenylcarbamoyl chloride (0.379 g, 2.24 mmol). The reaction
mixture was stirred under nitrogen atmosphere at 0°C for 30
15 min then at room temperature for 1h. The reaction was
monitored by TLC (5% methanol in dichloromethane). The
solvent was removed under reduced pressure and the residue was
washed with 10% citric acid and extracted with EtOAc. The

organic extracts were combined, washed with water dried over anhydrous Na_2SO_4 , and filtered. The solvent was removed under reduced pressure to afford a yellow syrup. The residue was purified by flash chromatography (silica gel) using 5% MeOH in CH_2Cl_2 to give the desired product (0.382g, 61%) as a white semisolid.

MS and ^1H -NMR were consistent with the desired structure. ^1H -NMR (d_6 -DMSO, 400 MHz) δ : 7.8 (d, 1H), 7.39 (m, 10H), 6.19 (s, 2H), 5.03 (s, 2H), 3.29 (s, 3H); HR-MS (ES) m/z calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3$ (MH^+) = 335.1396, observed 335.1418.

Step B

1-benzyl-3-bromo-2-oxo-1,2-dihydropyridin-4-yl methyl (phenyl) carbamate



15

To a solution of 1-benzyl-2-oxo-1,2-dihydropyridin-4-yl methyl (phenyl) carbamate (0.38 g, 1.13 mmol) in anhydrous CH_2Cl_2 (7 mL) was added N-Bromosuccinimide (NBS, 0.24 g, 1.34 mmol). The reaction was stirred overnight at room temperature under nitrogen atmosphere. The reaction mixture was purified by flash chromatography (silica gel) using EtOAc/hexanes (1:1 v/v). The appropriate fractions were collected according to ES MS ($\text{M}+\text{H}$ 413) and concentrated. The dried product showed about 14% of di-brominated product by analytical HPLC. The compounds were separated by reverse phase HPLC using a 10-90% acetonitrile in water, 30 min gradient at a 100 mL/min flow rate, to afford (after lyophilization) the salt of the desired compound. The salt was diluted in EtOAc and washed with NaHCO_3 . The organic extracts were dried over anhydrous Na_2SO_4 ,

25

filtered, and concentrated to afford the desired compound (0.271 g, 58%) as a beige solid.

MS and $^1\text{H-NMR}$ were consistent with the desired structure.

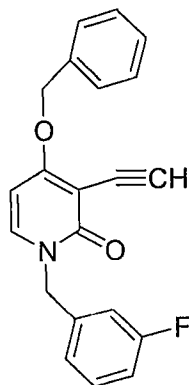
$^1\text{H-NMR}$ (d_6 -DMSO, 400Hz) δ : 7.83 (d, 1H), 7.39 (m, 10H), 6.48

5 (s, 1H), 5.12 (s, 2H), 3.33 (s, 3H); HR-MS (ES) m/z calcd for $\text{C}_{20}\text{H}_{17}\text{O}_3\text{Br}$ (MH^+) = 413.0495, observed 413.0496.

Example 57

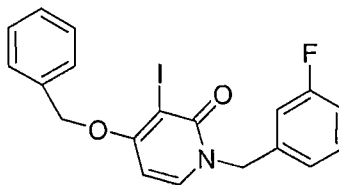
4-(benzyloxy)-3-ethynyl-1-(3-fluorobenzyl)pyridin-2(1H)-

10 one



Step A

Preparation of 4-(benzyloxy)-1-(3-fluorobenzyl)-3-iodopyridin-2(1H)-one



15

Heated a reaction mixture of 4-(benzyloxy)-1-(3-fluorobenzyl)pyridin-2(1H)-one (4.83 g, 15.6 mmol) in anhydrous acetonitrile (55 mL) and N-iodosuccinimide (NIS, 3.86 g, 17.1 mmol) under nitrogen atmosphere at 65° C for 4 h.

20 The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (silica gel) using EtOAc/hexanes (1:1 v:v). The appropriate fractions were collected according to ES MS ($\text{M}+\text{H}$ 436) and washed with

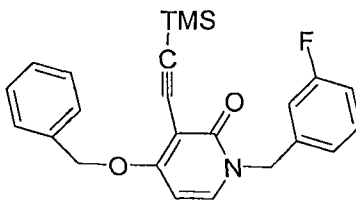
Na₂SO₃ to remove the color impurities. The fractions were concentrated under reduced pressure and dried in vacuo to afford the desired product (6.15 g, 90%) as a light yellow solid.

5 MS and ¹H-NMR were consistent with the desired structure. ¹H-NMR (CD₃OD, 400Hz) δ: 7.73 (d, 1H), 7.47 (d, 2H), 7.39 (m, 4H), 7.08 (m, 3H), 6.39 (d, 1H), 5.29 (s, 2H), 5.19 (s, 2H); HR-MS (ES) m/z calcd for C₁₉H₁₅NO₂FI (MH⁺) = 436.0210, observed 436.0196.

10

Step B

Preparation of 4-(benzyloxy)-1-(3-fluorobenzyl)-3-[(trimethylsilyl)ethynyl]pyridin-2(1H)-one



15 Degassed a solution of 4-(benzyloxy)-1-(3-fluorobenzyl)-3-iodopyridin-2(1H)-one (2.01 g, 4.62 mmol) in anhydrous acetonitrile (25 mL) under argon atmosphere. Triethylamine (1.11 g, 11 mmol) was added and quickly degassed. The reaction mixture was chilled in an ice bath for 15 minutes
20 before adding bistriphenylphosphine-palladium chloride (0.34 g, 0.48 mmol) and cuprous iodide (0.2 g). The reaction was stirred at room temperature for 30 min before heating at 60° C under an atmosphere of argon for 2 h. The reaction mixture was filtered through a bed of celite and the filtrate was
25 concentrated under reduced pressure. The dark brown residue was diluted with CH₂Cl₂ (100 mL) and washed with water. The organic extracts were combined, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The dark brown residue was purified by flash chromatography (silica

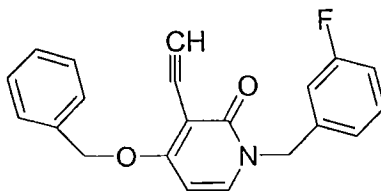
gel) using 30% EtOAc in hexane. The appropriate fractions were combined and concentrated under reduced pressure to afford the desired product (1.34 g, 72%) as a light yellow solid.

5 MS and ^1H -NMR were consistent with the desired structure. ^1H -NMR (CD_3OD , 400Hz) δ : 7.74 (d, 1H), 7.47 (d, 2H), 7.35 (m, 4H), 7.09 (m, 3H), 6.46 (d, 1H), 5.26 (s, 2H), 5.13 (s, 2H), 0.18 (s, 9H); HR-MS (ES) m/z calcd for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{FSi}$ (MH^+) = 406.1638, observed 406.1610.

10

Step C

Preparation of 4-(benzyloxy)-3-ethynyl-1-(3-fluorobenzyl)pyridin-2(1H)-one



15 To a solution of 4-(benzyloxy)-1-(3-fluorobenzyl)-3-[(trimethylsilyl)ethynyl]pyridin-2(1H)-one (1.31 g, 3.2 mmol) in anhydrous acetonitrile (25 mL) at 0° C was added tetrabutylammonium fluoride (0.611g, 1.93 mmol). The reaction was stirred at 0° C for 15 min then for 1 h at room
20 temperature. The reaction was concentrated under reduced pressure and the residue was diluted with EtOAc and washed with water. The organic extracts were combined, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography
25 (silica gel) using EtOAc in hexanes (1:1 v/v). The appropriate fractions were combined and concentrated under reduced pressure to afford the desired product (0.779 g, 72%) as a gold solid.

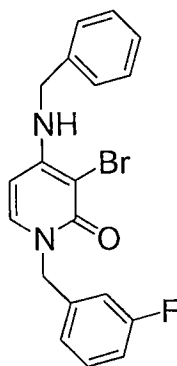
MS and ^1H -NMR were consistent with the desired structure.

^1H -NMR (CD_3OD , 400Hz) δ : 7.73 (d, 1H), 7.43 (d, 2H), 7.35 (m, 4H), 7.09 (m, 3H), 6.45 (d, 1H), 5.27 (s, 2H), 5.13 (s, 2H), 3.78 (s, 1H); HR-MS (ES) m/z calcd for $\text{C}_{21}\text{H}_{16}\text{NO}_2\text{F}$ (MH^+) =

5 334.1243, observed 334.1234.

Example 58

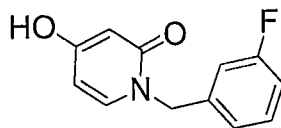
4-(benzylamino)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one



10

Step A

Preparation of 1-(3-fluorobenzyl)-4-hydroxypyridin-2(1H)-one



15

In a Fischer-Porter bottle, added a solution of 4-(benzyloxy)-1-(3-fluorobenzyl)pyridin-2(1H)-one (4.5 g, 14.56 mmol) in absolute ethanol (20 mL). Flushed the solution with nitrogen then added palladium catalyst (1.05 g). Sealed bottle and evacuated system. The system was purged with hydrogen gas (2 X 15 psi) to check for leaks. The reaction was charged with hydrogen (35 psi) and stirred at room temperature for 45 min. The system was evacuated and flushed with nitrogen. The reaction was filtered and the catalyst was carefully washed with fresh ethanol. The filtrate was concentrated under reduced pressure.

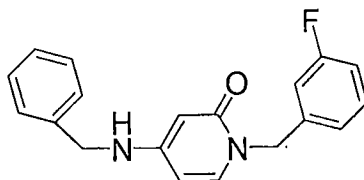
25

MS and ^1H -NMR were consistent with the desired structure.
 ^1H -NMR (CD_3OD , 400Hz) δ : 7.54 (d, 1H), 7.32 (m, 1H), 7.06 (m, 3H), 6.05 (dd, 1H), 5.83 (s, 1H), 5.09 (s, 2H); HR-MS (ES) m/z calcd for $\text{C}_{12}\text{H}_{10}\text{NO}_2\text{F}$ (MH^+) = 220.0774, observed 220.0787.

5

Step B

Preparation of 4-(benzylamino)-1-(3-fluorobenzyl)pyridin-2(1H)-one

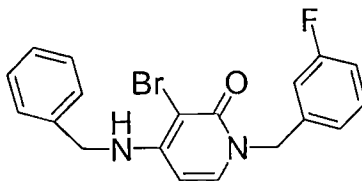


10 Heated a reaction mixture of 1-(3-fluorobenzyl)-4-hydroxypyridin-2(1H)-one (1.005 g, 4.5 mmol) in benzylamine (15 mL) at reflux (185° C) under nitrogen atmosphere for 24 h. The reaction was monitored by ES-MS (MH^+ 309). The solvent was removed by vacuum distillation to give a yellow residue.

15 MS and ^1H -NMR were consistent with the desired structure.
 ^1H -NMR (CD_3OD , 400Hz) δ : 7.31 (m, 7H), 7.03 (m, 3H), 5.98 (dd, 1H), 5.45 (s, 1H), 5.00 (s, 2H), 4.30 (s, 2H); HR-MS (ES) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{N}_2\text{OF}$ (MH^+) = 309.1403, observed 309.1375.

20 Step C

Preparation of 4-(benzylamino)-3-bromo-1-(3-fluorobenzyl)pyridin-2(1H)-one

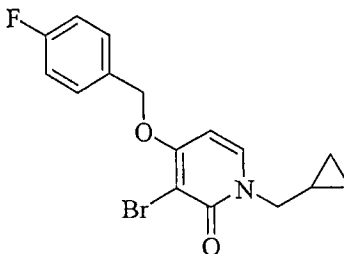


25 To a solution of 4-(benzylamino)-1-(3-fluorobenzyl)pyridin-2(1H)-one (0.50 g, 1.62 mmol) in anhydrous CH_2Cl_2 (10 mL) was added N-bromosuccinimide (NBS, 0.30 g, 1.7 mmol). The reaction was stirred at room

temperature under a nitrogen atmosphere for 3 h. The reaction mixture was purified by flash chromatography (silica gel) using EtOAc in hexanes (1:1 v/v). The appropriate fractions were combined and concentrated.

5 MS and ^1H -NMR were consistent with the desired structure. ^1H -NMR (CD_3OD , 400Hz) δ : 7.41 (d, 1H), 7.31 (m, 6H), 7.04 (m, 3H), 5.99 (d, 1H), 5.08 (s, 2H), 4.53 (s, 2H); HR-MS (ES) m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}\text{FBr}$ (MH^+) = 387.0508, observed 387.0504.

10 Example 59



3-Bromo-1-cyclopropylmethyl-4-(4-fluorobenzoyloxy)-
1H-pyridin-2-one

15 Step 1. Preparation of 4-[(4-Fluorobenzoyloxy)pyridine-1-oxide.

To an ice-cold solution of sodium hydride (1.9 g, of a 60% dispersion in mineral oil, 46 mmol) in DMF (39 mL) was added 4-fluorobenzyl alcohol (5.1 mL, 46 mmol). The reaction

20 mixture was warmed to room temperature, 4-chloropyridine-1-oxide¹ (5.0 g, 39 mmol) was added, and the reaction mixture was stirred for 6 h. The reaction mixture was diluted with a 50% aqueous solution of brine, and extracted with CHCl_3 (7 x 50 mL). The combined organics were dried (MgSO_4), filtered, and
25 concentrated under reduced pressure. Trituration with Et_2O afforded 4-[(4-fluorobenzoyloxy)pyridine-1-oxide as an off-white solid (9.1 g, 90%), which was used in the next step without further purification or characterization.

Step 2. Preparation of 4-(4-Fluorobenzoyloxy)-1H-pyridin-2-one.

A solution of 4-[(4-fluorobenzoyloxy)pyridine-1-oxide (6.4 g, 29 mmol) in acetic anhydride (97 mL) was heated at reflux for
5 3 h. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was diluted with 1:1 MeOH/water (34 mL), and the mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure. Trituration with Et₂O/hexanes afforded
10 4-(4-fluorobenzoyloxy)-1H-pyridin-2-one as a brown solid (3.1 g, 48%): ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.36 (m, 2H), 7.22 (d, J = 8 Hz, 1H), 7.09 (t, J = 7 Hz, 2H), 6.03 (dd, J = 7, 3 Hz, 1H), 5.94 (d, J = 3 Hz, 1H), 4.98 (s, 2H).

15 Step 3. Preparation of 3-Bromo-4-(4-fluorobenzoyloxy)-1H-pyridin-2-one.

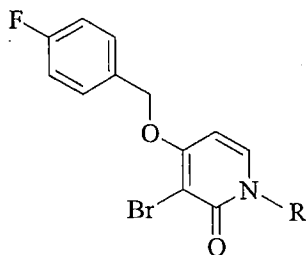
To an ice-cold solution of 4-(4-fluorobenzoyloxy)pyridine-2(1H)-one (3.1 g, 14 mmol) in AcOH (26 mL) was added a solution of bromine (0.79 mL, 15 mmol) in AcOH (51 mL), and
20 the reaction mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, and purification by flash column chromatography (silica, 1:1 Et₂O/hexanes) to afford 3-bromo-4-(4-fluorobenzoyloxy)-1H-pyridin-2-one as an orange solid (0.78 g, 48%): MS APCI m/z
25 298 [M + H]⁺.

Step 4. Preparation of 3-Bromo-1-cyclopropylmethyl-4-(4-fluorobenzoyloxy)-1H-pyridin-2-one.

To a solution of 3-bromo-4-(4-fluorobenzoyloxy)-1H-pyridin-2-one (0.25 g, 0.84 mmol) in DMF (13 mL) was added K₂CO₃ (0.33 g, 1.7 mmol) and cyclopropylmethyl bromide (0.14 g, 1.0 mmol), and the reaction mixture was stirred at 110 °C for 2 h. The reaction mixture was cooled to room temperature, and the

solvent was removed under reduced pressure. The residue was diluted with a 50% aqueous solution of brine, and extracted with CHCl_3 (3 x 50 mL). The combined organics were washed with water and then brine, dried (MgSO_4), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 EtOAc/hexanes) afforded 3-bromo-1-cyclopropyl-methyl-4-(4-fluorobenzyloxy)-1H-pyridin-2-one as a yellow solid (0.12 g, 39%): mp 139-141 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.43-7.34 (m, 3H), 7.07 (t, J = 9 Hz, 2H), 6.06 (d, J = 6 Hz, 1H), 5.19 (s, 2H), 3.82 (d, J = 9 Hz, 2H), 1.26-1.23 (m, 1H), 0.62-0.57 (m, 2H), 0.40-0.36 (m, 2H). ESHRMS m/z 352.0368 ($\text{M}+\text{H}$ $\text{C}_{16}\text{H}_{16}\text{BrFNO}_2$ requires 352.0343)

Examples 60-69



The compounds of Examples 60-69 are prepared essentially according to the procedures set forth above for Example 59.

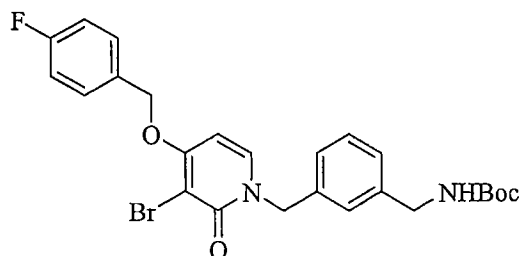
Example No.	R	MF	M+H Requires	ESHRMS m/z
Ex. 60	pyridin-4-ylmethyl			
Ex. 61	pyridin-3-ylmethyl	$\text{C}_{18}\text{H}_{14}\text{BrFN}_2\text{O}_2$	489.0296	489.0281
Ex. 62	4-tert-butylbenzyl	$\text{C}_{23}\text{H}_{23}\text{BrFNO}_2$	444.0969	444.0971
Ex. 63	3-trifluoromethylbenzyl	$\text{C}_{20}\text{H}_{14}\text{BrF}_4\text{NO}_2$	456.0217	456.0202

Ex. 64	Biphenyl-2-ylmethyl	C ₂₅ H ₁₉ BrFNO ₂	464.0656	464.0656
Ex. 65	4-methoxybenzyl	C ₂₀ H ₁₇ BrFNO ₃	418.0449	418.0457
Ex. 66	4-cyanobenzyl	C ₂₀ H ₁₄ BrFN ₂ O ₂	413.0295	413.0287
Ex. 67	4-trifluoromethylbenzyl	C ₂₀ H ₁₄ BrF ₄ NO ₂	456.0217	456.0192
Ex. 68	Biphenyl-4-ylmethyl	C ₂₅ H ₁₉ BrFNO ₂	464.0656	464.0653
Ex. 69	cyclohexylmethyl	C ₁₉ H ₂₁ BrFNO ₂	394.0812	394.0797

NMR characterization of compounds of Examples 12-19

Ex. No.	NMR Data
Ex. 60	¹ H NMR (300 MHz, CDCl ₃) δ 8.57 (dd, <i>J</i> = 6, 3 Hz, 2H), 7.43-7.38 (m, 2H), 7.16 (d, <i>J</i> = 6 Hz, 2H), 7.09 (t, <i>J</i> = 9 Hz, 2H), 6.12 (d, <i>J</i> = 6 Hz, 1H), 5.20 (s, 2H), 5.16 (s, 2H)
Ex. 61	¹ H NMR (300 MHz, CDCl ₃) δ 8.58-8.55 (m, 2H), 7.75 (d, <i>J</i> = 6 Hz, 1H), 7.41-7.37 (m, 2H), 7.31-7.26 (m, 2H), 7.12-7.04 (m, 2H), 5.17 (d, <i>J</i> = 6 Hz, 1H), 5.18 (s, 2H), 5.16 (s, 2H)
Ex. 62	¹ H NMR (300 MHz, MeOD) δ 7.75 (d, 1H, <i>J</i> = 9 Hz), 7.59 (t, <i>J</i> = 9 Hz, 2H), 7.37 (d, <i>J</i> = 9 Hz, 2H), 7.22 (d, <i>J</i> = 9 Hz, 2H), 7.06-6.99 (m, 2H), 6.52 (d, <i>J</i> = 9 Hz, 1H), 5.29 (s, 2H), 5.18 (s, 2H), 1.28 (s, 9H)
Ex. 63	¹ H NMR (300 MHz, CDCl ₃) δ 7.58-7.37 (m, 5H), 7.29-7.26 (m, 2H), 7.08 (t, <i>J</i> = 7 Hz, 2H), 6.10 (d, <i>J</i> = 7 Hz, 1H), 5.20 (s, 2H), 5.18 (s, 2H)
Ex. 64	¹ H NMR (300 MHz, CDCl ₃) δ 7.42-7.27 (m, 11H), 7.07 (t, <i>J</i> = 6 Hz, 2H), 6.72 (d, <i>J</i> = 7 Hz, 1H), 5.88 (d, <i>J</i> = 9 Hz, 1H), 5.16 (s, 2H), 5.12 (s, 2H)
Ex. 65	¹ H NMR (300 MHz, CDCl ₃) δ 7.38-7.36 (m, 2H), 7.27-6.84 (m, 3H), 7.08 (s, 2H), 6.86 (d, <i>J</i> = 7 Hz, 2H), 6.01 (d, <i>J</i> = 6 Hz, 1H), 5.15 (s, 2H), 5.09 (s, 2H), 3.78 (s, 3H)
Ex. 66	¹ H NMR (300 MHz, CDCl ₃) δ 7.64-7.61 (m, 2H), 7.42-7.37 (m, 4H), 7.27-7.25 (m, 1H), 7.12-7.06 (m, 2H), 6.11 (d, <i>J</i> = 6 Hz, 1H), 5.19 (s, 4H)
Ex. 67	¹ H NMR (300 MHz, CDCl ₃) δ 7.59 (d, <i>J</i> = 6 Hz, 2H), 7.43-7.37 (m, 4H), 7.29-7.25 (m, 1H), 7.08 (t, <i>J</i> = 6 Hz, 2H), 6.08 (d, <i>J</i> = 9 Hz, 1H), 5.20 (s, 2H), 5.18 (s, 2H)
Ex. 68	¹ H NMR (300 MHz, CDCl ₃) δ 7.57-7.54 (m, 4H), 7.45-7.34 (m, 7H), 7.30-7.26 (m, 1H), 7.08 (t, <i>J</i> = 9 Hz, 2H), 6.06 (d, <i>J</i> = 6 Hz, 1H), 5.20 (s, 2H), 5.17 (s, 2H)
Ex. 69	¹ H NMR (300 MHz, CDCl ₃) δ 7.93 (d, <i>J</i> = 6 Hz, 1H), 7.45-7.40 (m, 2H), 7.29-7.26 (m, 1H), 7.09 (t, <i>J</i> = 9 Hz, 2H), 6.50 (d, <i>J</i> = 6 Hz, 1H), 5.17 (s, 2H), 4.14 (d, <i>J</i> = 6 Hz, 2H), 1.90-1.74 (m, 5H), 1.32-1.05 (m, 5H)

Example 70



{3-[3-Bromo-4-(4-fluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzyl}carbamic acid *tert*-butyl ester

5

Step 1. Preparation of 3-Hydroxymethylbenzonitrile.

To an ice-cold solution of 3-cyanobenzaldehyde (5.0 g, 38 mmol) in 1:1 MeOH/THF (90 mL) was added NaBH₄ (1.6 g, 42 mmol), and the reaction mixture was stirred for 3 h. The reaction mixture was diluted with brine, and the solvent was removed under reduced pressure. The residue was dissolved in water, and the aqueous layer was extracted with Et₂O (3 x 100 mL). The combined organics were washed with brine, dried (MgSO₄), filtered, and concentrated under reduced pressure to provide 3-hydroxymethyl-benzonitrile (4.95 g, 98%) as a clear oil, which was used in the next step without further purification or characterization.

Step 2. Preparation of 3-(*tert*-Butyldimethylsilyloxymethyl)benzonitrile.

To an ice-cold solution of 3-hydroxymethyl benzonitrile (4.95 g, 37 mmol) in CH₂Cl₂ (47 mL) was added imidazole (5.1 g, 74 mmol), DMAP (0.45 g, 3.7 mmol), and TBSCl (6.2 g, 41 mmol), and the reaction mixture was stirred for 12 h. The reaction mixture was diluted with water, and the aqueous layer was extracted with CH₂Cl₂ (3 x 150 mL). The combined organics were washed with brine, dried (MgSO₄), filtered, and concentrated under reduced pressure to provide 3-(*tert*-butyldimethylsilyloxymethyl)-benzonitrile (9.1 g, 99%) as a

clear oil: ^1H NMR (300 MHz, CDCl_3) δ 7.51 (s, 1H), 7.42 (d, J = 6 Hz, 1H), 7.35-7.28 (m, 1H), 4.75 (s, 2H), 0.94 (s, 9H), 0.11 (s, 6H).

5 Step 3. Preparation of 3-(tert-Butyldimethylsilyloxymethyl)benzylamine.

To an ice-cold solution of 3-(tert-butyl-
butyldimethylsilyloxymethyl)benzonitrile (4.5 g, 18 mmol) in
THF (47 mL) was added LiAlH_4 (27 mL, of a 1 M solution in THF,
10 27 mmol), and the reaction mixture was stirred at reflux for 3
h. The reaction mixture was cooled to 0 °C, and the reaction
was quenched with water (25 mL) and 15%NaOH in water (75 mL).
The reaction mixture was filtered, concentrated under reduced
pressure, and the residue was dissolved in EtOAc. The organic
15 solution was washed with water and then brine, dried (MgSO_4),
filtered, and concentrated under reduced pressure to provide
3-(tert-Butyldimethylsilyloxymethyl)benzylamine (1.4 g, 30%)
as a clear oil: ^1H NMR (300 MHz, CDCl_3) δ 7.22-7.10 (m, 4H),
4.57 (s, 2H), 3.74 (s, 2H), 0.84 (s, 9H), 0.09 (s, 6H).

20

Step 4. Preparation of 3-(Hydroxymethyl)benzylcarbamic acid
tert-butyl ester.

To a solution of 3-(tert-
butyldimethylsilyloxymethyl)benzylamine (1.4 g, 5.5 mmol) and
25 Et_3N (1.5 mL, 11 mmol) in CH_2Cl_2 (28 mL) was added di-tert-
butyl dicarbonate (1.3 g, 5.8 mmol), and the reaction mixture
was stirred for 12 h. The reaction mixture was diluted with
water and extracted with CH_2Cl_2 (3 x 100 mL). The combined
organics were washed with brine, dried (MgSO_4), filtered, and
30 concentrated under reduced pressure. Purification by flash
column chromatography (silica, CH_2Cl_2) to afford 3-
(hydroxymethyl)benzylcarbamic acid tert-butyl ester as a
yellow oil (1.4 g, 46%): ^1H NMR (300 MHz, CDCl_3) δ 7.32-7.28

(m, 1H), 7.18 (d, $J = 8$ Hz, 1H), 7.12 (s, 1H), 7.08-7.01 (m, 1H), 4.60 (s, 2H), 4.04 (d, $J = 6$ Hz, 2H), 1.36 (s, 9H).

Step 5. Preparation of 3-(Bromomethyl)benzylcarbamic acid
5 tert-butyl ester.

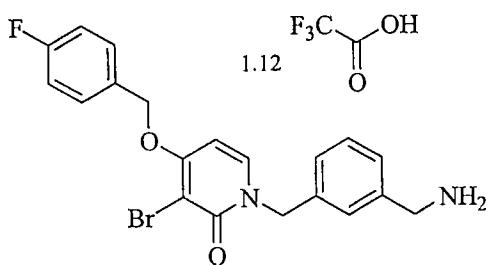
To an ice-cold solution of 3-(hydroxymethylbenzyl)carbamic acid tert-butyl ester (0.7 g, 3.0 mmol) and CBr_4 (1.0 g, 3.1 mmol) in THF (14 mL) was added Ph_3P (0.81 g, 3.1 mmol), and the reaction mixture was stirred
10 for 18 h. The reaction mixture was filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, eluent 5:95 to 15:85 EtOAc/hexanes) to afford the 3-(bromomethyl)benzyl-carbamic acid tert-butyl ester as a white solid (0.42 g, 51%): ^1H NMR (300 MHz, MeOD) δ
15 7.55 (s, 1H), 7.32-7.27 (m, 2H), 7.21-7.19 (m, 1H), 4.54 (s, 2H), 4.21 (s, 2H), 1.28 (s, 9H).

Step 6. Preparation of 1{3-[3-Bromo-4-(4-fluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzyl}carbamic acid tert-butyl
20 ester.

To a solution of 3-bromo-4-(4-fluorobenzyloxy)pyridine-2(1H)-one (from Step 3, synthesis EXAMPLE 59) (0.2 g, 0.67 mmol) in DMF (11 mL) was added K_2CO_3 (0.26 g, 1.3 mmol) and 3-(bromomethyl)benzylcarbamic acid tert-butyl ester (0.23 g, 0.80 mmol), and the reaction mixture was stirred at 80 °C for
25 3 hours. The reaction mixture was cooled to room temperature, and concentrated under reduced pressure. The residue was diluted with a 50% aqueous solution of brine (24 mL), and extracted with CHCl_3 (4 x 50 mL). The combined organics was
30 washed with water and then brine, dried (MgSO_4), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 3:7 EtOAc/hexanes) and recrystallization from MeOH afforded {3-[3-bromo-4-(4-

fluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzyl}carbamic acid tert-butyl ester as an off-white solid (0.07 g, 20%): mp 136-138 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.37 (m, 2H), 7.30-7.20 (m, 5H), 7.08 (t, *J* = 9 Hz, 2H), 6.04 (d, *J* = 9 Hz, 1H), 5.16 (s, 2H), 5.14 (s, 2H), 4.28 (d, *J* = 6 Hz, 1H), 1.44 (s, 9H). ESHRMS *m/z* 517.1124 (M+H C₂₅H₂₇BrFN₂O₄ requires 517.1133)

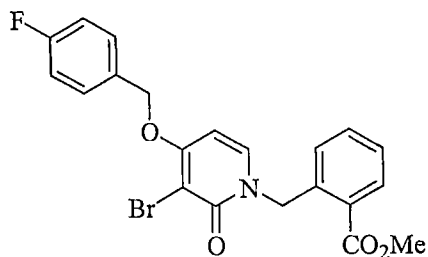
Example 71



1-(3-Aminomethylbenzyl)-3-bromo-4-(4-fluorobenzyloxy)-1H-pyridin-2-one

To an ice-cold solution of 1-[3-{N-tert-Butoxycarbonyl}aminomethylbenzyl]-3-bromo-4-(4-fluorobenzyloxy)pyridine-2(1H)-one (Example 69) (0.05 g, 0.1 mmol) in CH₂Cl₂ (2 mL) was added TFA (2 mL), and the reaction mixture was stirred for 1 h. The solvent was removed under reduced pressure to provide 1-(3-aminomethylbenzyl)-3-bromo-4-(4-fluorobenzyloxy)-1H-pyridin-2-one as a tan solid (0.049 g, 100%), as the TFA salt: mp 127-139 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.13 (br s, 2H), 7.94 (d, *J* = 6 Hz, 1H), 7.52-7.47 (m, 2H), 7.44-7.37 (m, 2H), 7.27 (t, *J* = 8 Hz, 3H), 6.53 (d, *J* = 8 Hz, 1H), 5.30 (s, 2H), 5.14 (s, 2H), 4.01 (d, *J* = 6 Hz, 2H), 3.39 (br s, 2H); Anal. Calcd for C₂₀H₁₇BrF₂N₂O₂•1.125 TFA: C, 48.99; H, 3.53; N, 5.13. Found: C, 48.80; H, 3.43; N, 4.75. ESHRMS *m/z* 417.0608 (M+H C₂₀H₁₉BrFN₂O₂ requires 417.0609).

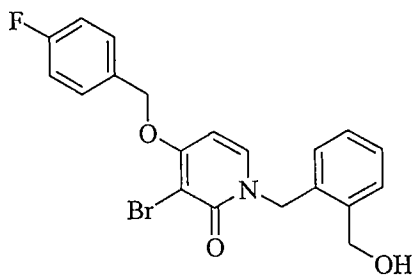
Example 72



5 Methyl 2-[3-Bromo-4-(4-fluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzoate

The title compound was prepared by a procedure similar to the one described for EXAMPLE 59 (0.36 g, 48%): mp 161-165 °C; ¹H
 10 NMR (300 MHz, CDCl₃) δ 7.98 (d, *J* = 6 Hz, 1H), 7.51-7.26 (m, 6H), 7.11-7.05 (m, 2H), 6.05 (d, *J* = 8 Hz, 1H), 5.60 (s, 2H), 5.18 (s, 2H), 3.93 (s, 3H). ESHRMS *m/z* 446.0430 (M+H)
 C₂₁H₁₈BrFNO₄ requires 418.0398)

15 Example 73



3-Bromo-4-(4-fluorobenzoyloxy)-1-(2-hydroxymethylbenzyl)-
 1H-pyridin-2-one

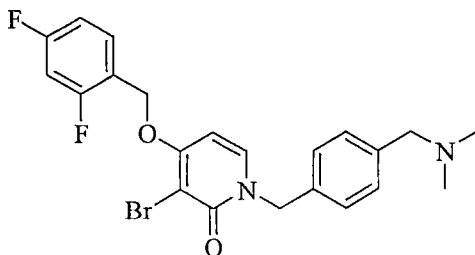
20

To an ice-cold solution of 3-bromo-4-(4-fluorobenzoyloxy)-1-(2-hydroxymethylbenzyl)-1H-pyridin-2-one (Example 72) (0.25 g, 0.56 mmol) in THF (1 mL) was added LiBH₄ (2.0 M solution in THF, 0.56 mmol), and the reaction mixture was stirred at 40 °C

for 6 hours. The reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure, and the residue was dissolved in EtOAc. The organic solution was washed with brine, dried (MgSO₄), filtered, and

concentrated under reduced pressure. ¹H NMR (300 MHz, DMSO-d₆) δ 7.82 (d, *J* = 8 Hz, 1H), 7.54-7.49 (m, 2H), 7.41 (d, *J* = 7 Hz, 1H), 7.29-7.21 (m, 4H), 6.81 (d, *J* = 7 Hz, 1H), 6.53 (d, *J* = 8 Hz, 1H), 5.30-5.25 (m, 3H), 5.18 (s, 2H), 4.60 (d, *J* = 7 Hz, 2H). ESHRMS *m/z* 418.0437 (M+H C₂₀H₁₈BrFNO₃ requires 418.0449)

Example 74



3-Bromo-4-(2,4-difluorobenzoyloxy)-1-[(4-dimethylaminomethyl)benzyl]-1H-pyridin-2-one

Step 1. Preparation of 4-(2,4-Difluorobenzoyloxy)pyridine-1-oxide.

To an ice-cold solution of sodium hydride (1.2 g of a 60% dispersion in mineral oil, 51 mmol) in DMF (43 mL) was added 2,4-difluorobenzyl alcohol (5.7 mL, 51 mmol). The reaction mixture was warmed to room temperature, 4-chloropyridine-1-oxide¹ (5.5 g, 43 mmol) was added, and the reaction mixture was stirred for 6 h. The reaction mixture was diluted with a 50% aqueous solution of brine, and extracted with CHCl₃ (7 x 50 mL). The combined organics were dried (MgSO₄), filtered, and the solvent was removed under reduced pressure. Trituration with Et₂O afforded 4-(2,4-difluorobenzoyloxy)pyridine-1-oxide as an off-white solid (9.1 g, 90%): ¹H NMR (300 MHz, CDCl₃) δ

8.16-8.08 (m, 1H), 7.47-7.36 (m, 1H), 6.97-6.81 (m, 1H), 5.09 (d, $J = 8$ Hz, 1H).

Step 2. Preparation of 4-(2,4-Difluorobenzoyloxy)-1H-pyridin-2-one.

A solution of 4-(2,4-difluorobenzoyloxy)pyridine-1-oxide (13.4 g, 57 mmol) in acetic anhydride (30 mL) was stirred at reflux for 4 h. The solvent was removed under reduced pressure, the residue was diluted with 1:1 MeOH/water (60 mL), and the mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure. Purification by flash column chromatography (silica, eluent methylene chloride to 9:1 methylene chloride/methanol) provided 4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one as a light brown solid (4.2 g, 31%): ^1H NMR (300 MHz, CDCl_3) δ 7.43 (q, $J = 8$ Hz, 1H), 7.23 (d, $J = 7$ Hz, 1H), 6.91-6.87 (m, 2H), 6.02 (dd, $J = 8, 2$ Hz, 1H), 5.97 (d, $J = 2$ Hz, 1H), 5.03 (s, 2H).

Step 3. Preparation of 3-Bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one.

To an ice-cold solution of 4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one (0.75 g, 3.1 mmol) in AcOH (12 mL) was added a solution of bromine (0.2 mL, 3.5 mmol) in AcOH (6 mL), and the reaction mixture was stirred 10 min. The solvent was removed under reduced pressure to afford 3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one as a white solid (1.0 g, 100%): ESI MS m/z 299 $[\text{M} + \text{H}]^+$.

Step 4. Preparation of 3-Bromo-1-(4-chloromethylbenzyl)-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one.

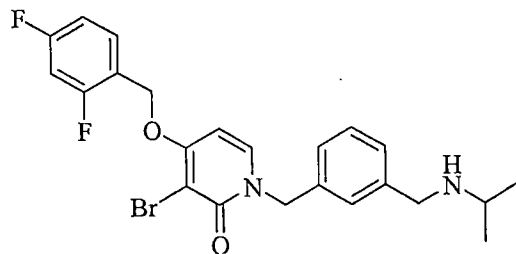
To a solution of 3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one (0.60 g, 2.5 mmol) in DMF (40 mL) was added K_2CO_3 (0.70 g, 5.1 mmol) and α,α' -dichloro-*p*-xylene (0.53 g, 3.0 mmol), and

the reaction mixture was stirred at 110 °C for 2 h. The reaction mixture was cooled to room temperature, diluted with brine, and extracted with CHCl₃ (4 x 100 mL). The combined organics were washed water and then brine, dried (Na₂SO₄),
5 filtered, and concentrated under reduced pressure to afford 3-bromo-1-(4-chloromethylbenzyl)-4-(2,4-difluorobenzyloxy)-1H-pyridin-2-one as an off-white solid (0.49 g, 43%): ¹H NMR (300 MHz, CDCl₃) δ 7.54 (app q, *J* = 8 Hz, 1H), 7.38-7.28 (m, 5H), 6.94 (td, *J* = 8, 2 Hz, 1H), 6.85 (td, *J* = 8, 2 Hz, 1H), 6.10
10 (d, *J* = 9 Hz, 1H), 5.21 (s, 2H), 5.16 (s, 2H), 4.56 (s, 2H).

Step 5. Preparation of 3-Bromo-4-(2,4-difluorobenzyloxy)-1-[(4-dimethylaminomethyl) benzyl]-1H-pyridin-2-one.

To a sealed tube containing 3-bromo-1-(4-chloromethylbenzyl)-4-(2,4-difluoro-benzyloxy)-1H-pyridin-2-one (0.49 g, 1.1 mmol)
15 was added a solution of dimethylamine (5.5 mL of a 2.0 M solution in THF, 11 mmol), and the reaction mixture was stirred for 15 h. The solvent was removed under reduced pressure. Purification by flash column chromatography
20 (silica, eluent methylene chloride to 92:7.2:0.8 methylene chloride/methanol/ammonia) provided 3-bromo-4-(2,4-difluorobenzyloxy)-1-(4-dimethylaminomethylbenzyl)-1H-pyridin-2-one as a light yellow solid (0.23 g, 46%): mp 111-113 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.50-7.49 (m, 1H), 7.26-7.22 (m, 5H),
25 6.90-6.88 (m, 1H), 6.82-6.78 (m, 1H), 6.04 (d, *J* = 6 Hz, 1H), 5.16 (s, 2H), 5.11 (s, 2H), 3.37 (s, 2H), 2.19 (s, 6H). ESHRMS *m/z* 463.0782 (M+H C₂₂H₂₂BrF₂N₂O₂ requires 463.0827)

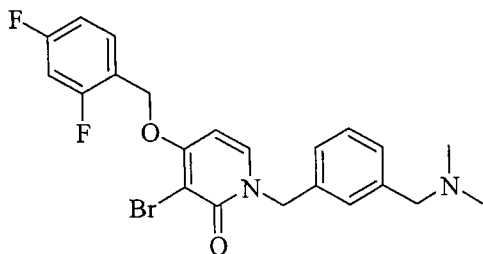
Example 75



3-Bromo-4-(2,4-difluorobenzoyloxy)-1-[3-(isopropylaminomethyl)benzyl]-1H-pyridin-2-one

5 The title compound was prepared by a procedure similar to the one described for Example 74 (0.06 g, 35%): mp 109-110 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.54 (d, *J* = 6 Hz, 1H), 7.33-7.20 (m, 5H), 6.94-6.81 (m, 2H), 6.10 (d, *J* = 6 Hz, 1H), 5.20 (s, 2H), 5.14 (s, 2H), 3.77 (s, 2H), 2.88 (t, *J* = 6 Hz, 1H), 1.13 (d, *J* = 6 Hz, 6H). ESHRMS *m/z* 477.0955 (M+H C₂₃H₂₄BrF₂N₂O₂ requires 477.0984)

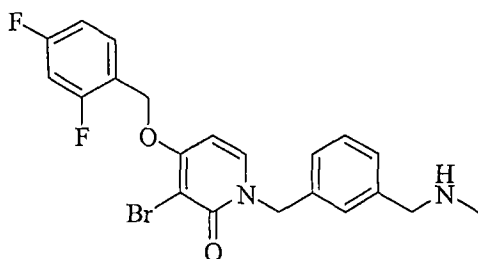
Example 76



15 3-Bromo-4-(2,4-difluorobenzoyloxy)-1-[(3-dimethylaminomethyl)benzyl]-1H-pyridin-2-one

20 The title compound was prepared by a procedure similar to the one described for Example 74 (0.06 g, 25%): mp 103-107 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.52 (d, *J* = 8 Hz, 1H), 7.32-7.24 (m, 5H), 6.94 (td, *J* = 9, 3 Hz, 1H), 6.84 (td, *J* = 9, 3 Hz, 1H), 6.08 (d, *J* = 8 Hz, 1H), 5.20 (s, 2H), 5.16 (s, 2H), 3.44 (s, 2H), 2.24 (s, 6H). ESHRMS *m/z* 463.0801 (M+H C₂₂H₂₂BrF₂N₂O₂ requires 463.0827).

Example 77

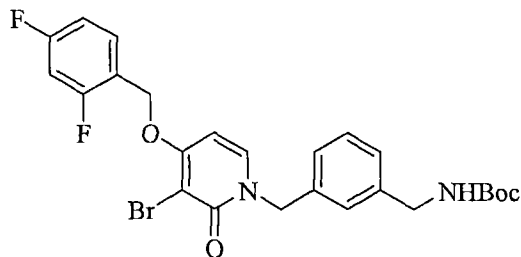


3-Bromo-4-(2,4-difluorobenzoyloxy)-1-[(3-methylaminomethyl)benzyl]-1H-pyridin-2-one

5

The title compound was prepared by a procedure similar to the one described for Example 74 (0.05 g, 16%): mp 107-111 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.55 (d, *J* = 6 Hz, 1H), 7.31-7.19 (m, 5H), 6.94-6.81 (m, 2H), 6.09 (d, *J* = 6 Hz, 1H), 5.20 (s, 2H), 5.14 (s, 2H), 3.73 (s, 2H), 2.45 (s, 1H). ESHRMS *m/z* 449.0652 (M+H C₂₁H₂₀BrF₂N₂O₂ requires 449.0671)

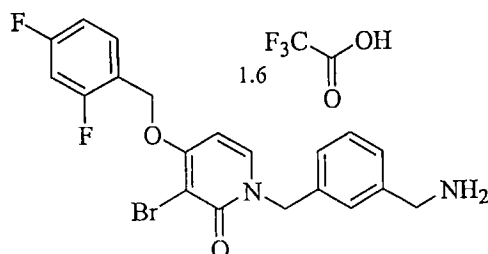
Example 78



{3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzyl}carbamic acid tert-butyl ester

The title compound was prepared essentially according to the procedure described in Example 70. mp 80-84 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.60-7.50 (m, 1H), 7.33-7.21 (m, 5H), 6.97-6.81 (m, 2H), 6.10 (dd, *J* = 8, 2 Hz, 1H), 5.20 (s, 2H), 5.15 (s, 2H), 4.87 (br s, 2H), 4.30 (s, 2H) 1.45 (s, 9H). ESHRMS *m/z* 535.1019 (M+H C₂₅H₂₆BrF₂N₂O₄ requires 535.1039)

Example 79

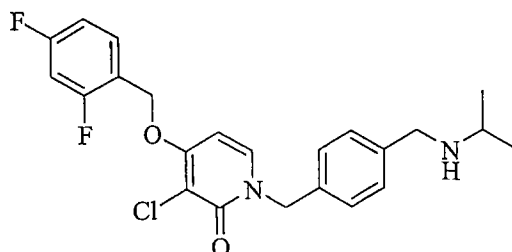


1-[(3-Aminomethyl)benzyl]-3-bromo-4-(2,4-difluorobenzoyloxy)-
1H-pyridin-2-one

Step 1. Preparation of 1-[(3-Aminomethyl)benzyl]-3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one.

To an ice-cold solution of {3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzyl}carbamic acid tert-butyl ester (Example 78) (0.05 g, 0.1 mmol) in CH₂Cl₂ (2 mL) was added TFA (2 mL), and the reaction mixture was stirred for 1 hour. The solvent was removed under reduced pressure to provide 1-[(3-aminomethyl)benzyl]-3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one as a tan solid (0.049 g, 100%), as the TFA salt: mp 80-84 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.15 (br s, 3H), 7.97 (d, *J* = 8 Hz, 1H), 7.79-7.60 (m, 1H), 7.44-7.30 (m, 4H), 7.20-7.15 (m, 1H), 6.61 (d, *J* = 6 Hz, 1H), 5.31 (s, 2H), 5.16 (s, 2H), 4.03 (s, 2H); ¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -74.56 (4.8F), -109.63 (1F), -113.61 (1F). ESHRMS *m/z* 435.0540 (M+H C₂₀H₁₈BrF₂N₂O₂ requires 435.0515)

Example 80



3-Chloro-4-(2,4-difluorobenzoyloxy)-1-[4-(isopropylaminomethyl)benzyl]-1H-pyridin-2-one

Step 1. Preparation of 3-Chloro-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one.

To a solution of 4-[(4-fluorobenzyl)oxy]pyridine-2(1H)-one (from Step 2, Example 74) (1.4 g, 5.9 mmol) in AcOH (25 mL) was added N-chlorosuccinimide (0.95 g, 7.1 mmol) and the reaction mixture was heated at reflux for 2 h. The solvent was removed under reduced pressure. ¹H NMR (300 MHz, MeOD) δ 7.63-7.55 (m, 1H), 7.45(d, J = 8 Hz, 1H), 7.07-7.00 (m, 2H), 6.58 (d, J = 8 Hz, 1H), 5.31 (d, J = 8 Hz, 1H).

Step 2. Preparation of 3-Chloro-1-(4-chloromethylbenzyl)-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one.

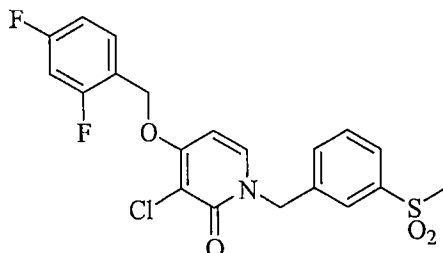
3-Chloro-1-(4-chloromethylbenzyl)-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one was prepared by procedure similar to the one described for 3-bromo-1-(4-chloromethylbenzyl)-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one (Step 3,) as white solid (0.24 g, 34%): ¹H NMR (300 MHz, CDCl₃) δ 7.53 (app q, J = 9 Hz, 1H), 7.34 (app q, J = 9 Hz, 1H), 7.23 (d, J = 8 Hz, 1H), 6.94 (td, J = 10, 2 Hz, 1H), 6.85 (td, J = 10, 2 Hz, 1H), 6.14 (d, J = 8 Hz, 1H), 5.20 (s, 2H), 5.16 (s, 2H), 4.56 (s, 2H).

Step 3. Preparation of 3-Chloro-4-(2,4-difluorobenzoyloxy)-1-[4-(isopropylamino-methyl)benzyl]-1H-pyridin-2-one.

The title compound was prepared by a procedure similar to the one described for Example 74 (0.17 g, 69 %): mp 146-151 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.52 (app q, J = 9 Hz, 1H), 7.35-7.21 (m, 5H), 6.94 (td, J = 8, 2 Hz, 1H), 6.85 (td, J = 8, 2 Hz, 1H), 6.18 (d, J = 8 Hz, 1H), 5.22 (s, 2H), 5.08 (s, 2H),

3.81 (s, 2H), 2.98 (br s, 1H), 1.20 (s, 6H). ESHRMS m/z
433.1481 (M+H C₂₃H₂₄ClF₂N₂O₂ requires 433.1489)

Example 81



5 3-Chloro-4-(2,4-difluorobenzoyloxy)-1-[(3-methanesulfonyl)benzyl]-1H-pyridin-2-one

Step 1. Preparation of (3-Methanesulfonyl)phenyl methanol.

To an ice-cold solution of 3-(methylsulfonyl)benzoic acid (1.4
10 g, 7.1 mmol) in 2:1 Et₂O/THF (60 mL) was added LiAlH₄ (8.5 mL
of 1.0 M solution in THF, 8.5 mmol), and the reaction mixture
was heated at reflux for 1 h. The reaction mixture was cooled
to 0 °C, and the reaction was quenched with water (15 mL) and
15%NaOH in water (35 mL). The reaction mixture was filtered,
15 concentrated under reduced pressure, and the residue was
dissolved in EtOAc. The organic solution was washed with
water and then brine, dried (MgSO₄), filtered, and concentrated
under reduced pressure. Purification by flash column
chromatography (silica, eluent 1:2 to 3:1 EtOAc/hexanes)
20 provided (3-methanesulfonyl)phenyl methanol as a clear oil
(0.56 g, 42%): ¹H NMR (300 MHz, CDCl₃) δ 7.93 (s, 1H), 7.83 (d,
J = 7 Hz, 1H), 7.64 (d, J = 7 Hz, 1H), 7.53 (t, J = 7 Hz, 1H),
4.78 (d, J = 6 Hz, 2H), 3.05 (s, 3H), 2.61 (br s, 1H).

25 Step 2. Preparation of 1-Chloromethyl-3-methanesulfonylbenzene.

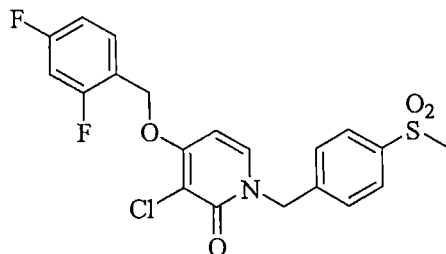
A solution of (3-methanesulfonyl)phenyl methanol (0.21 g, 1.1
mmol) in thionyl chloride (3 mL) was heated at 80 °C for 3 h.
The reaction mixture was cooled to room temperature, and the

solvent was removed under reduced pressure to provide 1-chloromethyl-3-methanesulfonylbenzene as a yellow oil (0.23 g, 95%): ^1H NMR (300 MHz, CDCl_3) δ 7.98 (s, 1H), 7.90 (d, $J = 8$ Hz, 1H), 7.70 (d, $J = 8$ Hz, 1H), 7.59 (t, $J = 8$ Hz, 1H), 4.65 (s, 2H), 3.08 (s, 3H).

Step 3. Preparation of 3-Chloro-4-(2,4-difluorobenzyloxy)-1-[(3-methanesulfonyl)-benzyl]-1H-pyridin-2-one.

The title compound was prepared by a procedure similar to the one described for Example 80 (0.14 g, 78%): mp 155-157 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.88 (d, $J = 8$ Hz, 1H), 7.83 (m, 1H), 7.67 (d, $J = 8$ Hz, 1H), 7.58-7.48 (m, 2H), 7.31 (d, $J = 8$ Hz, 1H), 6.95-6.83 (m, 2H), 6.22 (d, $J = 8$ Hz, 1H), 5.22 (s, 4H), 3.08 (s, 3H). ESHRMS m/z 440.0525 ($\text{M}+\text{H}$ $\text{C}_{20}\text{H}_{17}\text{ClF}_2\text{NO}_4\text{S}$ requires 440.0529)

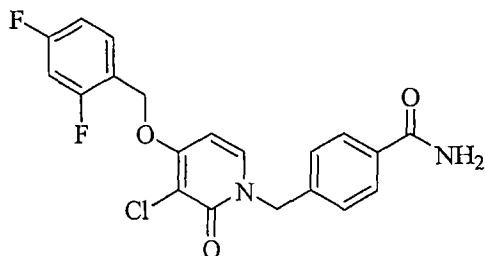
Example 82



3-Chloro-4-(2,4-difluorobenzyloxy)-1-[(4-methanesulfonyl)benzyl]-1H-pyridin-2-one

The title compound was prepared by a procedure similar to the one described for Example 81 (0.08 g, 73%): mp 223-225 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.91 (d, $J = 8$ Hz, 2H), 7.53-7.47 (m, 3H), 7.30-7.26 (m, 1H), 6.94-6.86 (m, 2H), 6.22 (d, $J = 8$ Hz, 1H), 5.23 (s, 4H), 3.03 (s, 3H). ESHRMS m/z 440.0512 ($\text{M}+\text{H}$ $\text{C}_{20}\text{H}_{17}\text{ClF}_2\text{NO}_4\text{S}$ requires 440.0529)

Example 83



4-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzamide

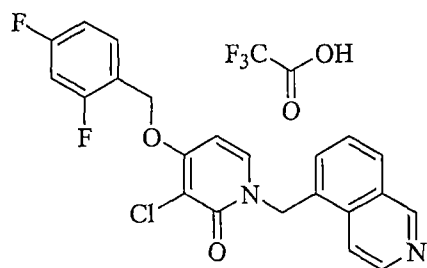
5 Step 1. Preparation of Methyl 4-[3-chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzoate.

Methyl 4-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzoate was prepared by a procedure similar to the one described for Example 81 (0.14 g, 60%): ¹H NMR (300 MHz, CDCl₃) δ 8.01 (dd, *J* = 8, 2 Hz, 1H), 7.52 (app q, *J* = 8 Hz, 1H), 7.36 (d, *J* = 9 Hz, 2H), 7.26-7.22 (m, 2H), 6.94 (td, *J* = 8, 2 Hz, 1H), 6.85 (td, *J* = 8, 2 Hz, 1H), 6.16 (d, *J* = 9 Hz, 1H), 5.21 (s, 4H), 3.92 (s, 3H).

15 Step 2. Preparation of 4-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzamide.

A sealed tube containing a solution of 4-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzoic acid methyl ester (0.25 g, 0.60 mmol) and NH₃ (20 mL of a 7 N solution in MeOH, 140 mmol) was heated at 75 °C for 16 h. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. Trituration with Et₂O/MeOH afforded 4-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzamide as a white solid (0.14 g, 60%): mp 235-238 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.93 (d, *J* = 8 Hz, 2H), 7.79 (d, *J* = 8 Hz, 2H), 7.60 (app q, *J* = 8 Hz, 1H), 7.35-7.27 (m, 4H), 7.20-7.10 (m, 1H), 6.61 (d, *J* = 8 Hz, 1H), 5.28 (s, 2H), 5.14 (s, 2H). ESHRMS *m/z* 405.0788 (M+H C₂₀H₁₆ClF₂N₂O₃ requires 405.0812)

Example 84



5

3-Chloro-4-(2,4-difluorobenzoyloxy)-1-isoquinolin-5-ylmethyl-
1H-pyridin-2-one

Step 1. Preparation of Isoquinolin-5-ylmethanol.

10 To an ice-cold solution of isoquinoline-5-carbaldehyde² (0.68 g, 4.3 mmol) in MeOH (15 mL) was added NaBH₄ (0.17 g, 4.6 mmol), and the reaction mixture was stirred for 15 min. The reaction was quenched with brine, the solvent was removed under reduced pressure, and the residue was dissolved in
15 EtOAc. The organic solution was washed with water and then brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure to afford isoquinolin-5-ylmethanol as a brown solid (0.63 g, 93%): ¹H NMR (300 MHz, DMSO-d₆) δ 9.87 (s, 1H), 8.82 (d, J = 6 Hz, 1H), 8.57 (d, J = 6 Hz, 1H), 8.47 (d, J = 9 Hz, 1H), 8.30 (d, J = 6 Hz, 1H), 7.95 (t, J = 9 Hz, 1H), 5.34 (s, 2H).
20

Step 2. Preparation of 5-Bromomethylisoquinoline.

To a solution of isoquinolin-5-ylmethanol (0.63 g, 3.9 mmol)
25 in AcOH (3.3 mL) was added HBr (6.6 mL, a 30% w/w solution in AcOH, 24 mmol), and the reaction mixture was stirred at 75 °C for 45 min. The reaction mixture was cooled to room temperature, and the precipitate was collected to provide the

5-bromomethylisoquinoline hydrobromide acid salt as a brown solid (1.1 g, 87%): ^1H NMR (300 MHz, CDCl_3) δ 9.22 (s, 1H), 8.58 (d, $J = 6$ Hz, 1H), 7.95-7.89 (m, 2H), 7.76 (d, $J = 9$ Hz, 1H), 7.59 (dd, $J = 9, 6$ Hz, 1H), 5.16 (s, 2H).

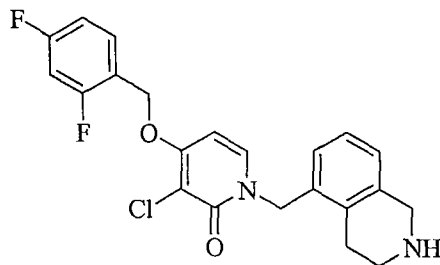
5

Step 3. Preparation of 3-Chloro-4-(2,4-difluorobenzoyloxy)-1-isoquinolin-5-ylmethyl-1H-pyridin-2-one.

The title compound was prepared by a procedure similar to the one described for Example 81, as the TFA salt (0.13 g, 33%):

10 mp 235-238 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 9.55 (s, 1H), 8.66 (d, $J = 6$ Hz, 1H), 8.29 (d, $J = 6$ Hz, 1H), 8.22 (d, $J = 8$ Hz, 1H), 7.91 (d, $J = 8$ Hz, 1H), 7.77 (t, $J = 8$ Hz, 1H), 7.65-7.63 (m, 1H), 7.53 (d, $J = 7$ Hz, 1H), 7.35-7.25 (m, 1H), 7.20-7.10 (m, 1H), 6.68 (d, $J = 8$ Hz, 1H), 5.67 (s, 2H), 5.32 (s, 2H);
 15 ^{19}F NMR (282 MHz, $\text{DMSO}-d_6$) δ -74.79 (3F), -109.43 (1F), -113.62 (1F). ESHRMS m/z 413.0868 ($\text{M}+\text{H}$ $\text{C}_{22}\text{H}_{16}\text{ClF}_2\text{N}_2\text{O}_3$ requires 413.0863)

Example 85



20

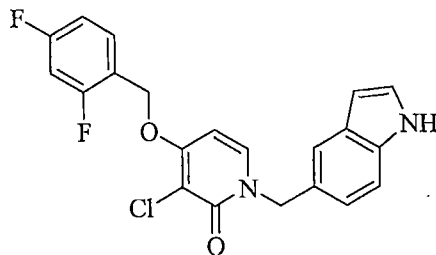
3-Chloro-4-(2,4-difluorobenzoyloxy)-1-(1,2,3,4-tetrahydroisoquinolin-5-ylmethyl)-1H-pyridin-2-one

Step 1. Preparation of 3-Chloro-4-(2,4-difluorobenzoyloxy)-1-(1,2,3,4-tetrahydro-isoquinolin-5-ylmethyl)-1H-pyridin-2-one.

25 To a solution of 3-chloro-4-(2,4-difluorobenzoyloxy)-1-isoquinolin-5-ylmethyl-1H-pyridin-2-one (Example 84) (0.14 g, 0.34 mmol) in AcOH (1.3 mL) was added NaCNBH_3 (0.09 g, 1.4 mmol), and the reaction mixture was stirred for 2 h. The

reaction mixture was cooled to 0 °C, and diluted with water (10 mL) and 40% aqueous NaOH (10 mL), and the aqueous layer was washed with EtOAc (3 x 50 mL). The combined organics were washed with brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, eluent 98:1.8:0.2 to 88:10.8:1.2 CH₂Cl₂/MeOH/NH₃) provided 3-chloro-4-(2,4-difluoro-benzyloxy)-1-(1,2,3,4-tetrahydroisoquinolin-5-ylmethyl)-1H-pyridin-2-one as a white solid (0.13 g, 92%): mp 180-184 °C; ¹H NMR (300 MHz, MeOD) δ 7.65-7.55 (m, 2H), 7.16-7.00 (m, 4H), 6.90-6.80 (m, 1H), 6.60 (d, *J* = 8 Hz, 1H), 5.31 (s, 2H), 5.20 (s, 2H), 4.06 (s, 2H), 3.21 (t, *J* = 6 Hz, 2H), 2.82 (t, *J* = 6 Hz, 2H). ESHRMS *m/z* 417.1173 (M+H C₂₂H₂₀ClF₂N₂O₂ requires 417.1176)

Example 86



3-Chloro-4-(2,4-difluorobenzyloxy)-1-(1H-indol-5-ylmethyl)-1H-pyridin-2-one

Step 1. Preparation of 5-(Carboxymethyl)-indole-1-carbamic acid *tert*-butyl ester.

To a solution of methyl indole-5-carboxylate (6.9 g, 39 mmol) and Et₃N (6.0 mL, 43 mmol) in CH₂Cl₂ (150 mL) was added di-*tert*-butyl dicarbonate (19 g, 86 mmol), and the reaction mixture was stirred for 14 h. The reaction mixture was diluted with CH₂Cl₂, washed with water and then brine, dried (Na₂SO₄), filtered, and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica, 3:7 EtOAc/hexanes) provided 5-(carboxymethyl)-indole-

1-carbamic acid *tert*-butyl ester as a light yellow oil (11 g, 100%): ^1H NMR (300 MHz, CDCl_3) δ 8.29 (s, 1H), 8.15 (d, J = 9 Hz, 1H), 7.93 (d, J = 9 Hz, 1H), 7.78 (d, J = 3 Hz, 1H), 6.85 (d, J = 3 Hz, 1H), 3.91 (s, 3H), 1.68 (s, 9H).

5

Step 2. Preparation of 5-Hydroxymethylindole-1-carbamic acid *tert*-butyl ester.

To a -78°C solution of 5-(carboxymethyl)-indole-1-carbamic acid *tert*-butyl ester (10.8 g, 39 mmol) in THF (180 mL) was
10 added DIBAL (127 mL of a 1 M solution in THF, 127 mmol), and the reaction mixture was stirred for 2.5 h. The reaction was quenched with 1:1 1 N HCl/MeOH (100 mL), the reaction mixture was warmed to room temperature, diluted with CH_2Cl_2 (100 mL), and separated. The organic solution was washed with saturated
15 Rochelle salt, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 EtOAc/hexanes) provided 5-hydroxymethylindole-1-carbamic acid *tert*-butyl ester as a yellow oil (6.5 g, 68%): ^1H NMR (300 MHz, CDCl_3) δ 8.07 (d, J = 9 Hz, 1H), 7.59 (d, J = 6
20 Hz, 1H), 7.54 (s, 1H), 7.28 (d, J = 9 Hz, 1H), 6.58 (d, J = 6 Hz, 1H), 4.73 (s, 2H), 1.97 (s, 9H).

Step 3. Preparation of 5-Bromomethylindole-1-carbamic acid *tert*-butyl ester.

25 To an ice-cold solution of 5-hydroxymethylindole-1-carbamic acid *tert*-butyl ester (0.51 g, 2.1 mmol) in 4:1 $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$ (4 mL) was added PBr_3 (0.2 mL, 2.2 mmol), and the reaction mixture was stirred for 40 min. The reaction mixture was diluted with CH_2Cl_2 , washed a saturated solution of NaHCO_3 (3 x 10 mL),
30 dried (Na_2SO_4), filtered, and the solvent was removed under reduced pressure to provide 5-bromomethyl-indole-1-carbamic acid *tert*-butyl ester as a yellow solid (0.59 g, 93%). ^1H NMR (300 MHz, CDCl_3) δ 8.07 (d, J = 9 Hz, 1H), 7.68-7.62 (m, 2H),

7.33 (d, $J = 9$ Hz, 1H), 6.60 (s, 1H), 4.68 (s, 2H), 1.67 (s, 9H).

Step 4. Preparation of 5-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]indole-1-carbamic acid tert-butyl ester.

5-[3-Chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]indole-1-carbamic acid tert-butyl ester was prepared by a procedure similar to the one described for Example 81 as an off-white solid (0.54 g, 67%): ^1H NMR (300 MHz, CDCl_3) δ 8.10 (d, $J = 8$ Hz, 1H), 7.60 (d, $J = 3$ Hz, 2H), 7.52 (m, 1H), 7.26 (m, 1H), 6.94 (td, $J = 9, 2$ Hz, 1H), 6.84 (td, $J = 9, 2$ Hz, 1H), 6.53 (d, $J = 2$ Hz, 1H), 6.08 (d, $J = 8$ Hz, 1H), 5.25 (s, 2H), 5.18 (s, 2H), 1.66 (s, 9H).

Step 5. Preparation of 3-Chloro-4-(2,4-difluorobenzoyloxy)-1-(1H-indol-5-ylmethyl)-1H-pyridin-2-one.

A flask containing 5-[3-chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]indole-1-carbamic acid tert-butyl ester (0.48 g, 0.96 mmol) was heated at 150 °C for 4 h. The reaction mixture was cooled to room temperature, and purification by preparatory HPLC (Phenomenex Luna C18(2)

column, 250 x 21.20 mm, 10 μ

Solvent A: 0.05% TFA in 95:5 $\text{H}_2\text{O}/\text{CH}_3\text{CN}$; Solvent B: 0.05% TFA in

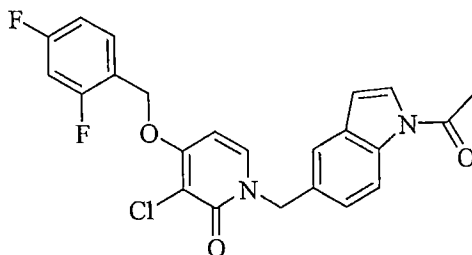
95:5 $\text{CH}_3\text{CN}/\text{H}_2\text{O}$

Eluent: 30-95% B over 20 min; flow 20.0 mL/min; UV Detector: 254 nm; Retention Time: 15.6 min) provided 3-chloro-4-(2,4-difluorobenzoyloxy)-1-(1H-indol-5-ylmethyl)-1H-pyridin-2-one as an off-white solid (0.14 g, 36%): mp 152-153 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 11.11 (br s, 1H), 7.91 (d, $J = 8$ Hz, 1H), 7.61 (app q, $J = 8$ Hz, 1H), 7.51 (s, 1H), 7.36-7.33 (m, 3H), 7.16 (td, $J = 8, 2$ Hz, 1H), 7.09 (dd, $J = 8, 2$ Hz, 1H), 6.57 (d, J

= 8 Hz, 1H), 6.40 (br s, 1H), 5.28 (s, 2H), 5.16 (s, 2H).
 ESHRMS m/z 401.0845 (M+H C₂₁H₁₆ClF₂N₂O₂ requires 401.0863).

Example 87

5



10

1-(1-Acetyl-1H-indol-5-ylmethyl)-3-chloro-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one

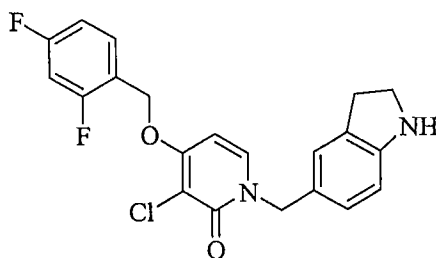
15

To a solution of 3-chloro-4-(2,4-difluorobenzoyloxy)-1-(1H-indol-5-ylmethyl)-1H-pyridin-2-one (Step 5, synthesis of Example 86) (0.22 g, 0.57 mmol) in CH₃CN (10 mL) was added acetic anhydride (0.06 mL, 0.58 mmol) and Et₃N (2 mL) , and the reaction mixture was stirred at 86 °C for 6 h. The reaction mixture was cooled to room temperature, and partitioned between 1 N HCl and EtOAc. The organic solution was separated, washed with brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. ¹H NMR (300 MHz, MeOD) δ 8.35 (d, J = 9 Hz, 1H), 7.77 (d, J = 9 Hz, 1H), 7.70 (d, J = 3 Hz, 1H), 7.54 (s, 2H), 7.31 (d, J = 9 Hz, 1H), 7.01-6.99 (m, 2H), 6.66 (d, J = 3 Hz, 1H), 6.59 (d, J = 9 Hz, 1H), 5.29 (s, 4H), 2.63 (s, 3H). ESHRMS m/z 443.0965 (M+H C₂₃H₁₈ClF₂N₂O₃ requires 443.0969).

20

25

Example 88



3-Chloro-4-(2,4-difluorobenzoyloxy)-1-(2,3-dihydro-1H-indol-5-ylmethyl)-1H-pyridin-2-one

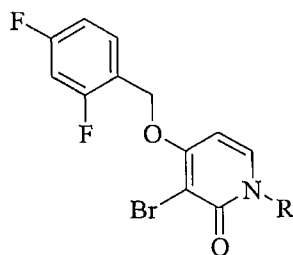
5

To a solution of 3-chloro-4-(2,4-difluorobenzoyloxy)-1-(1H-indol-5-ylmethyl)-1H-pyridin-2-one (Step 5, synthesis of Example 86) (0.24 g, 0.60 mmol) in AcOH (5 mL) was added NaCNBH₃ (0.06 g, 1.0 mmol), and the reaction mixture was
10 stirred for 1 h. The reaction mixture was partitioned between water and EtOAc, and the precipitate was collected by filtration. Trituration with CH₂Cl₂ afforded 3-Chloro-4-(2,4-difluorobenzyl-oxy)-1-(2,3-dihydro-1H-indol-5-ylmethyl)-1H-pyridin-2-one as a white solid (0.2 g, 81%): mp 137-139 °C; ¹H
15 NMR (300 MHz, CDCl₃) δ 7.51 (app q, *J* = 9 Hz, 1H), 7.21 (d, *J* = 6 Hz, 1H), 7.11 (s, 1H), 6.99-6.80 (m, 3H), 6.57 (d, *J* = 9 Hz, 1H), 6.08 (d, *J* = 9 Hz, 1H), 5.18 (s, 2H), 5.02 (s, 2H), 3.83 (br s, 1H), 3.55 (t, *J* = 9 Hz, 2H), 2.99 (t, *J* = 9 Hz, 2H). ESHRMS *m/z* 403.1022 (M+H C₂₁H₁₈ClF₂N₂O₂ requires 403.1019).

20

The following example compounds were prepared by procedures similar to that described for Example 74. The yields and the analytical data of the title compounds are reported below.

25 Examples 89-101.



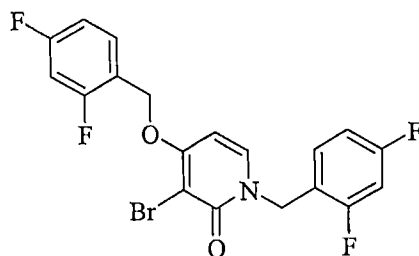
The compounds of Examples 89-101 are prepared essentially according to the procedures set forth above for Example 74.

5 The yield (Y), molecular formula (MF) and analytical data for these compounds are shown below.

Example No.	R	Y	MF	M+H Requires	ESHRMS m/z
Ex. 89	pyridin-3-ylmethyl	25	C ₁₈ H ₁₃ BrF ₂ N ₂ O ₂	407.0202	407.0197
Ex. 90	pyridin-4-ylmethyl	6	C ₁₈ H ₁₃ BrF ₂ N ₂ O ₂	407.0202	407.0189
Ex. 91	pyridin-2-ylmethyl	56	C ₁₈ H ₁₃ BrF ₂ N ₂ O ₂	407.0201	407.0184
Ex. 92	4- <i>tert</i> -butyl)benzyl	32	C ₂₃ H ₂₂ BrF ₂ NO ₂	462.0875	462.0863
Ex. 93	3-methoxybenzyl	50	C ₂₀ H ₁₆ BrF ₂ NO ₃	436.0354	436.0353
Ex. 94	Benzo[1,3]dioxol-5-ylmethyl	35	C ₂₀ H ₁₄ BrF ₂ NO ₄	450.0147	450.0136
Ex. 95	2-fluorobenzyl	42	C ₁₉ H ₁₄ BrF ₃ NO ₂	424.0155	424.0143

10 %): mp 179-182 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.58-7.53 (m, 3H), 7.33-7.26 (m, 1H), 7.14-7.02 (m, 2H), 6.96-6.82 (m, 2H), 6.11 (d, *J* = 9 Hz, 1H), 5.20 (s, 2H), 5.18 (s, 2H). ESHRMS m/z (M+H requires).

15 Example 96



3-Bromo-4-(2,4-difluorobenzoyloxy)-1-(2,4-difluorobenzyl)-1H-pyridin-2-one

5

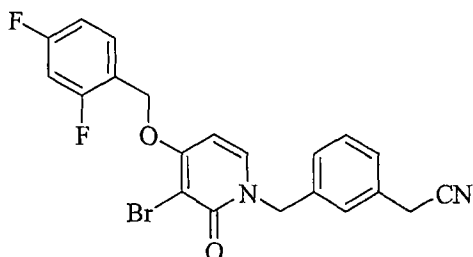
Step 1. Preparation of 4-(2,4-Difluorobenzoyloxy)-1-(2,4-difluorobenzyl)-1H-pyridin-2-one.

To a solution of 2,4-dihydroxypyridine (0.35 g, 3.2 mmol) in DMF (50 mL) was added K_2CO_3 (2.5 g, 13 mmol) and 2,4-difluorobenzyl bromide (1.0 mL, 7.6 mmol), and the reaction mixture was stirred at 110 °C for 4 h. The reaction mixture was cooled to room temperature, diluted with brine, and extracted with $CHCl_3$ (4 x 100 mL). The combined organics were washed with water and then brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. 1H NMR (300 MHz, $CDCl_3$) δ 7.54 (app q, J = 8 Hz, 1H), 7.38-7.28 (m, 5H), 6.94 (td, J = 8, 2 Hz, 1H), 6.85 (td, J = 8, 2 Hz, 1H), 6.10 (d, J = 9 Hz, 1H), 5.21 (s, 2H), 5.16 (s, 2H), 4.56 (s, 2H).

20 Step 2. Preparation of 3-Bromo-4-(2,4-difluorobenzoyloxy)-1-(2,4-fluorobenzyl)-1H-pyridin-2-one.

To an ice-cold solution of 4-(2,4-difluorobenzoyloxy)-1-(2,4-difluorobenzyl)-1H-pyridin-2-one (0.72 g, 2.0 mmol) in AcOH (4.0 mL) was added a solution of bromine (0.11 mL, 2.2 mmol) in AcOH (7.2 mL), and the reaction mixture was stirred for 40 min. The solvent was removed under reduced pressure. 1H NMR (300 MHz, $CDCl_3$) δ 7.63-7.45 (m, 2H), 7.42 (d, J = 6 Hz, 1H), 6.93-6.77 (m, 4H), 6.12 (d, J = 6 Hz, 1H), 5.20 (s, 2H), 5.12 (s, 2H). ERMS m/z $M+H$ 442.

Example 97



5 {3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2*H*-pyridin-1-ylmethyl]-phenyl}acetonitrile

Step 1. Preparation of Methyl 3-cyanomethylbenzoate.

To an ice-cold solution of methyl 3-bromomethylbenzoate (9.1
10 g, 40 mmol) in CH₃CN (108 mL) was added tetrabutylammonium
fluoride (17.3 mL, 60 mmol) and trimethylsilylcyanide (8.0 mL,
60 mmol), and the reaction mixture was heated at reflux for 20
h. The reaction mixture was cooled to room temperature, and
the solvent was removed under reduced pressure. Purification
15 by flash column chromatography (silica, 1:1 EtOAc/hexanes)
provided methyl 3-cyanomethylbenzoate as a clear oil (3.0 g,
43%): ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.97 (s, 1H), 7.92 (d, *J* = 8
Hz, 1H), 7.64 (d, *J* = 8 Hz, 1H), 7.56 (t, *J* = 8 Hz, 1H), 4.16
(s, 2H), 3.87 (s, 3H).

20

Step 2. Preparation of (3-Hydroxymethylphenyl)acetonitrile.

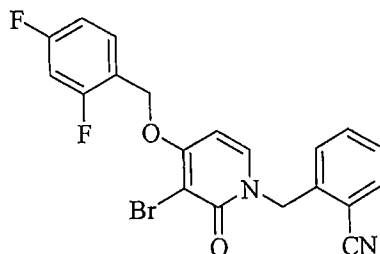
To an ice-cold solution of methyl 3-cyanomethylbenzoate (2.8
g, 18 mmol) in THF (23 mL) was added LiBH₄ (8.8 mL of a 2 M
solution in THF, 18 mmol), and the reaction mixture was heated
25 at reflux for 4 h. The reaction mixture was cooled to room
temperature, the reaction was quenched with 1:1 water/1 N HCl,
and the aqueous layer was washed with EtOAc (3 x 150 mL). The
combined organics were washed with brine, dried (MgSO₄),
filtered, and concentrated under reduced pressure.

Purification by flash column chromatography (silica, 2:1 EtOAc/hexanes) provided (3-hydroxymethylphenyl)-acetonitrile as a clear oil (0.97 g, 41%): ^1H NMR (300 MHz, MeOD) δ 8.15-8.08 (m, 1H), 7.47-7.34 (m, 1H), 7.27 (s, 1H), 6.97-6.82 (m, 1H), 4.87 (s, 2H), 3.91 (s, 2H)

Step 3. Preparation of (3-Bromomethylphenyl)acetonitrile.
To an ice-cold solution of (3-hydroxymethylphenyl)acetonitrile (0.97 g, 7.3 mmol) in THF (35 mL) was added CBr_4 (2.5 g, 7.7 mmol) and Ph_3P (2.0 g, 7.7 mmol), and the reaction mixture was stirred for 3 h. The reaction mixture was filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, eluent 1:9 to 1:4 EtOAc/hexanes) provided (3-bromomethylphenyl)acetonitrile as a clear oil (0.89 g, 58%): ^1H NMR (300 MHz, MeOD) δ 7.47-7.29 (m, 1H), 7.27 (s, 1H), 6.97-6.82 (m, 1H), 4.87 (s, 2H), 3.91 (s, 2H).

Step 4. Preparation of {3-[3-Bromo-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]phenyl}acetonitrile.
The title compound was prepared by a procedure similar to the one described for Example 74 (0.07 g, 10%): mp 120-121 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.60-7.50 (m, 1H), 7.37-7.27 (m, 5H), 6.96 (td, $J = 9, 3$ Hz, 1H), 6.82 (td, $J = 9, 3$ Hz, 1H), 6.13 (d, $J = 8$ Hz, 1H), 5.21 (s, 2H), 5.16 (s, 2H). ESHRMS m/z 445.0381 ($\text{M}+\text{H}$ $\text{C}_{21}\text{H}_{16}\text{BrF}_2\text{N}_2\text{O}_2$ requires 445.0358).

Example 98

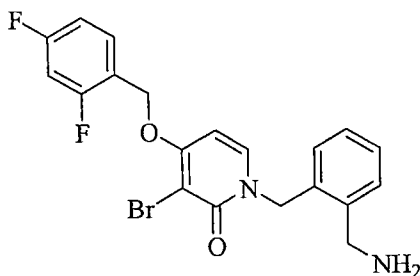


2-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzonitrile

5

The title compound was prepared by a procedure similar to the one described for Example 74 (0.13 g, 47%): mp 194-197 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.75 (d, *J* = 9 Hz, 1H), 7.69-7.49 (m, 4H), 7.42 (t, *J* = 8 Hz, 1H), 6.96-6.73 (m, 2H), 6.18 (d, *J* = 8 Hz, H), 6.17 (s, 2H), 5.30 (s, 2H). ESHRMS *m/z* 431.0210 (M+H C₂₀H₁₄BrF₂N₂O₂ requires 431.0201.

Example 99



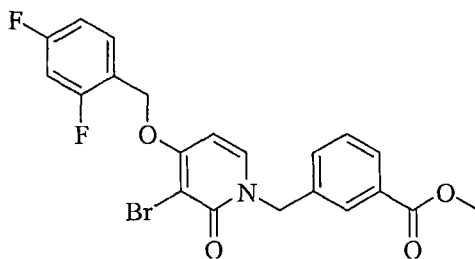
15

1-[(2-Aminomethyl)benzyl]-3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one

To a solution of 2-[3-bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzonitrile (0.11 g, 0.25 mmol) in THF (3 mL) was added BH₃·DMS (0.25 mL of a 2.0 M solution in THF, 0.5 mmol), and the reaction mixture was stirred at 70 °C for 1 h. The reaction mixture was cooled to 0 °C, and the reaction was quenched with MeOH. The solvent was removed under reduced

pressure, and the residue was partitioned between 2N NaOH and EtOAc. The organic solution was washed with brine, dried (MgSO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, eluent
 5 methylene chloride to 90:9:1 methylene chloride/methanol/ammonia) provided 1-[(2-aminomethyl)benzyl]-3-bromo-4-(2,4-difluorobenzoyloxy)-1*H*-pyridin-2-one as a white solid (0.15 g, 48%): ¹H NMR (300 MHz, CDCl₃) δ 7.55 (app q, *J* = 8 Hz, 1H), 7.40-7.26 (m, 4H), 7.14 (d, *J* = 8 Hz, 1H), 6.94
 10 (td, *J* = 8, 2 Hz, 1H), 6.85 (td, *J* = 8, 2 Hz, 1H), 6.08 (d, *J* = 8 Hz, 1H), 5.31 (s, 2H), 5.21 (s, 2H) 4.03 (s, 2H). ESHRMS *m/z* 435.0517 (M+H C₂₀H₁₈BrF₂N₂O₂ requires 435.0514).

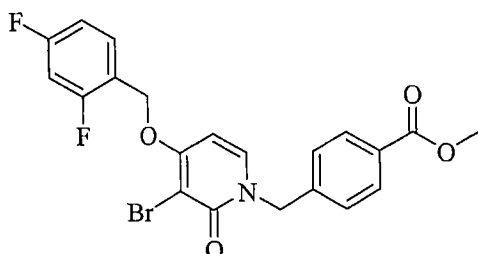
Example 100



Methyl 3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2*H*-pyridin-1-ylmethyl] benzoate

20 The title compound was prepared by a procedure similar to the one described for Example 74 (0.05 g, 11%): mp 115-117 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.15-7.95 (m, 2H), 7.65-7.50 (m, 2H), 7.45-7.40 (m, 1H), 7.32 (d, *J* = 6 Hz, 1H), 7.00-6.80 (m, 2H), 6.12 (d, *J* = 9 Hz, 1H), 5.21 (s, 2H), 5.20 (s, 2H), 3.92 (s,
 25 3H). ESHRMS *m/z* 464.0292 (M+H C₂₁H₁₇BrF₂NO₄ requires 464.0303).

Example 101



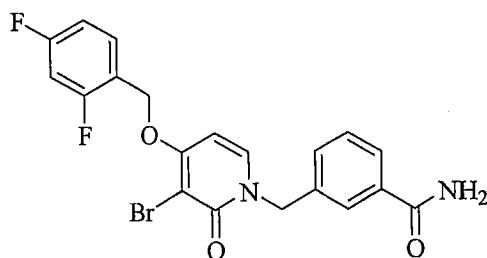
Methyl 4-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-benzoate

5

The title compound was prepared by a procedure similar to the one described for Example 74 (0.17 g, 46%): mp 136-139 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.01 (d, *J* = 8 Hz, 2H), 7.60-7.51 (m, 1H), 7.37 (d, *J* = 8 Hz, 2H), 7.29-7.26 (m, 1H), 6.93 (td, *J* = 9, 2 Hz, 1H), 6.84 (td, *J* = 9, 2 Hz, 1H), 6.13 (d, *J* = 8 Hz, 1H), 5.23 (s, 4H), 3.91 (s, 3H). ESHRMS *m/z* 464.0306 (M+H C₂₁H₁₇BrF₂NO₂ requires 464.0304).

Example 102

15



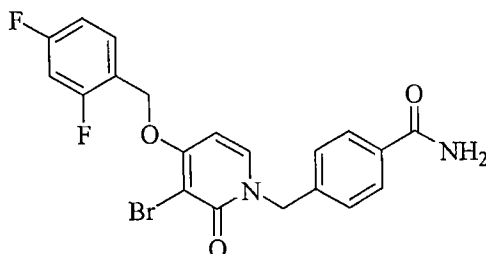
3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzamide

20 A sealed tube containing a solution of methyl 3-[3-bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzoate (0.1 g, 0.21 mmol) and NH₃ (3 mL of a 7 N solution in MeOH, 21 mmol) was heated at 75 °C for 16 h. The reaction mixture was cooled to room temperature and the solvent was removed under
25 reduced pressure. Trituration with Et₂O/MeOH afforded a white

solid (0.06 g, 64%): mp 198-201 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.02-8.00 (m, 2H), 7.85-7.75 (m, 2H), 7.70-7.60 (m, 1H), 7.45-7.30 (m, 4H), 7.17 (t, *J* = 3 Hz, 1H), 6.60 (d, *J* = 9 Hz, 1H), 5.32 (s, 2H), 5.18 (s, 2H). ESHRMS *m/z* 449.0295 (M+H

5 C₂₀H₁₆BrF₂N₂O₃ requires 449.0307).

Example 103



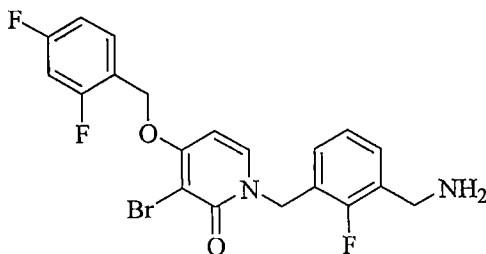
10 4-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]benzamide

The title compound was prepared by a procedure similar to the one described for Example 102 from Example 101 (0.04 g,

15 12%): mp 235-238 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.00 (d, *J* = 8 Hz, 1H), 7.94 (br s, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.64 (app q, *J* = 8 Hz, 1H), 7.38-7.30 (m, 4H), 7.17 (td, *J* = 6, 2 Hz, 1H), 6.60 (d, *J* = 9 Hz, 1H), 5.27 (s, 2H), 5.14 (s, 2H). ESHRMS *m/z* 449.0291 (M+H C₂₀H₁₆BrF₂N₂O₃ requires 449.0307).

20

Example 104



25 1-(3-Aminomethyl-2-fluorobenzyl)-3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one

Step 1. Preparation of 3-Bromo-1-(3-bromomethyl-2-fluorobenzyl)-4-(2,4-difluorobenzyloxy)-1*H*-pyridin-2-one.

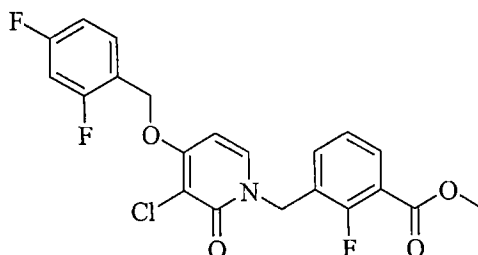
To a solution of 3-bromo-4-(2,4-difluorobenzyloxy)-1*H*-pyridin-2-one (from Step 3, Example 74) (0.3 g, 0.95 mmol) in DMF (26
5 mL) was added K₂CO₃ (0.26 g, 1.9 mmol) and 2,6-bis(bromomethyl)fluorobenzene (1.6 g, 5.7 mmol), and the reaction mixture was stirred at 110 °C for 3 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was diluted with
10 a 50% aqueous solution of brine, and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organics were washed with water, dried (Na₂SO₄), filtered, and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica, eluent 99:1 to 95:5 methylene
15 chloride/methanol) afforded 3-bromo-1-(3-bromomethyl-2-fluorobenzyl)-4-(2,4-difluorobenzyloxy)-1*H*-pyridin-2-one as an off-white solid (0.24 g, 49%): ¹H NMR (300 MHz, CDCl₃) δ 7.55-7.40 (m, 3H), 7.35-7.25 (m, 1H), 7.10-7.05 (m, 1H), 7.00-6.80 (m, 2H), 6.14 (d, *J* = 6 Hz, 1H), 5.22 (s, 2H), 5.19 (s, 2H),
20 4.50 (s, 2H).

Step 2. Preparation of 1-(3-Aminomethyl-2-fluorobenzyl)-3-bromo-4-(2,4-difluorobenzyloxy)-1*H*-pyridin-2-one.

A sealed tube containing a solution of 3-bromo-1-(3-bromomethyl-2-fluorobenzyl)-4-(2,4-difluorobenzyloxy)-1*H*-
25 pyridin-2-one (0.24 g, 0.45 mmol) and NH₃ (24 mL of a 7 N solution in MeOH, 168 mmol) was heated at 80 °C for 1 h. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. Purification by
30 flash column chromatography (silica, eluent 99.5:0.5 to 96:4 methylene chloride/methanol) afforded a white solid (0.12 g, 60%): mp 160-163 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.46-7.45 (m, 1H), 7.44-7.35 (m, 2H), 7.34-7.26 (m, 1 H), 7.15-7.05 (m, 1H),

6.95-6.80 (m, 2H), 6.11 (d, $J = 9$ Hz, 1H), 5.21 (s, 2H), 5.19 (s, 2H), 3.90 (s, 2H). ESHRMS m/z 453.0442 ($M+H$ $C_{20}H_{17}BrF_3N_2O_2$ requires 453.0420).

5 Example 105



Methyl 3-[3-chloro-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-2-fluorobenzoate

10

Step 1. Preparation of Methyl 2-fluoro-3-methylbenzoate.

To a solution of 2-fluoro-3-methyl benzoic acid (3.57 g, 23 mmol) in MeOH (40 mL) was added concentrated sulfuric acid (2.3 mL), and the reaction mixture was heated at reflux for 12

15 h. The reaction mixture was cooled, the solvent was removed under reduced pressure, and the residue was dissolved in EtOAc. The organic solution was washed with a saturated solution of $NaHCO_3$ and then brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford methyl 2-fluoro-3-methylbenzoate as a yellow oil (3.2 g, 82%): 1H NMR (300 MHz, $CDCl_3$) δ 7.76-7.71 (m, 1H), 7.39-7.34 (m, 1H), 7.08 (t, $J = 8$ Hz, 1H), 3.98 (s, 3H), 2.31 (d, $J = 3$ Hz, 3H).

20

Step 2. Preparation of Methyl 3-bromomethyl-2-fluorobenzoate.

25

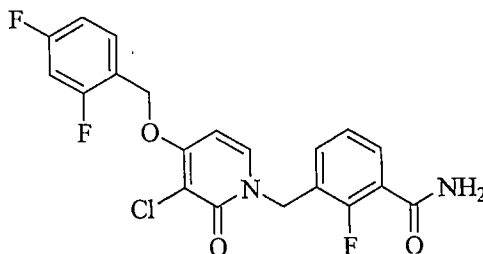
To a mixture of methyl 2-fluoro-3-methylbenzoate (1.5 g, 8.9 mmol) and N-bromosuccinimide (1.67 g, 9.4 mmol) was added carbon tetrachloride (24 mL) and benzoyl peroxide (5 mg), and the mixture was heated at reflux for 16 h. The reaction mixture was cooled, filtered, and concentrated under reduced

pressure. Purification by flash column chromatography (silica, eluent 5:95 to 60:40 EtOAc/hexanes) afforded methyl 3-bromomethyl-2-fluorobenzoate as a light yellow solid (0.91 g, 41%): ^1H NMR (300 MHz, CDCl_3) δ 7.93-7.88 (m, 1H), 7.61-7.56 (m, 1H), 7.20 (t, J = 8 Hz, 1H), 4.53 (d, J = 3 Hz, 2H), 3.94 (s, 3H).

Step 3. Preparation of Methyl 3-[3-chloro-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-2-fluorobenzoate.

Methyl 3-[3-chloro-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-2-fluorobenzoate was prepared by a procedure similar to the one described for Example 81 (0.33 g, 69%): mp 171-174 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.89-7.84 (m, 2H), 7.60-7.45 (m, 2H), 7.25-7.15 (m, 1H), 7.00-6.80 (m, 2H), 6.17 (d, J = 6.0 Hz, 1H), 5.21 (s, 2H), 5.19 (s, 2H), 3.93 (s, 3H). ESHRMS m/z 438.0747 ($M+H$ $\text{C}_{21}\text{H}_{16}\text{ClF}_3\text{NO}_4$ requires 438.0714).

Example 106



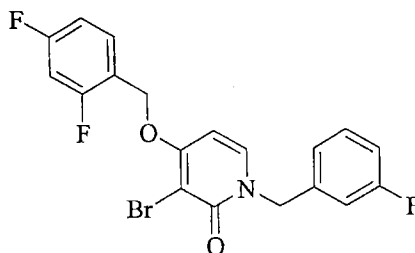
3-[3-Chloro-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-2-fluoro-benzamide

The title compound was prepared by a procedure similar to the one described for Example 99 (0.15 g, 62%): mp 252-254 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.04 (d, J = 8 Hz, 1H), 7.92 (br s, 1H), 7.79-7.65 (m, 3H), 7.49-7.48 (m, 1H), 7.37-7.31 (m, 3H),

6.80 (d, $J = 8$ Hz, 1H), 5.46 (s, 2H), 5.33 (s, 2H). ESHRMS
m/z 423.0710 (M+H $C_{20}H_{15}ClF_3N_2O_3$ requires 423.0718).

Example 107

5



3-Bromo-4-(2,4-difluorobenzoyloxy)-1-(3-fluorobenzyl)-1H-
pyridin-2-one

10

Step 1. Preparation of 4-Benzyloxy-1-(3-fluorobenzyl)-1H-pyridin-2-one.

To a solution of 4-benzyloxy-1H-pyridin-2-one (1.0 g, 5 mmol)
15 and K_2CO_3 (2.0 g, 9.9 mmol) in DMF (30 mL) was added 3-fluorobenzyl bromide (1.4 g, 7.5 mmol), and the reaction mixture was heated to 110 °C for 3 h. The reaction mixture was cooled to room temperature, and partitioned between EtOAc and water. The organic solution was washed with water and
20 then brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica, eluent 97:3 to 93:7 methylene chloride /methanol) afforded 4-benzyloxy-1-(3-fluorobenzyl)-1H-pyridin-2-one (1.04 g, 67%): 1H NMR (300 MHz, $CDCl_3$) δ 7.45-7.25 (m, 5H), 7.13 (d, $J = 8$ Hz, 1H), 7.10-6.90 (m, 3H), 6.10-5.95 (m, 2H), 5.07 (s, 2H), 5.00 (s, 2H).
25

Step 2. Preparation of 1-(3-Fluorobenzyl)-4-hydroxy-1H-pyridin-2-one.

To a solution of 4-benzyloxy-1-(3-fluorobenzyl)-1H-pyridin-2-one (1.79 g, 5.8 mmol) in EtOH (50 mL) was added 10% Pd/C (0.4 g), and reaction mixture was stirred under a hydrogen atmosphere for 1.5 h. The reaction mixture was filtered
5 through diatomaceous earth and concentrated under reduced pressure to give 1-(3-fluorobenzyl)-4-hydroxy-1H-pyridin-2-one (0.92 g, 72%): ^1H NMR (300 MHz, CDCl_3) δ 7.55 (d, J = 6 Hz, 1H), 7.40-7.30 (m, 1H), 7.10-6.95 (m, 3H), 6.07 (dd, J = 6, 3 Hz, 1H), 5.85 (d, J = 3 Hz, 1H), 5.11 (s, 2H).

10

Step 3. Preparation of 3-Bromo-1-(3-fluorobenzyl)-4-hydroxy-1H-pyridin-2-one.

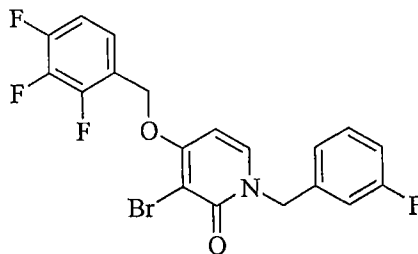
To an ice-cold solution of 1-(3-fluorobenzyl)-4-hydroxy-1H-pyridin-2-one (0.67 g, 3.1 mmol) in AcOH (5.7 mL) was added a
15 solution of bromine (0.52 g, 3.24 mmol) in AcOH (10.8 mL), and the reaction mixture was stirred for 5 min. The reaction mixture was warmed to room temperature and concentrated under reduced pressure to afford 3-bromo-1-(3-fluorobenzyl)-4-hydroxy-1H-pyridin-2-one as a yellow solid (1.07 g, crude): ^1H
20 NMR (500 MHz, MeOD) δ 7.64 (d, J = 8 Hz, 1H), 7.35-7.30 (m, 1H), 7.05-6.90 (m, 3H), 6.20 (d, J = 8 Hz, 1H), 5.18 (s, 2H).

Step 4. Preparation of 3-Bromo-4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one.

25 To a solution of 3-bromo-1-(3-fluorobenzyl)-4-hydroxy-1H-pyridin-2-one (0.20 g, 0.67) and K_2CO_3 (0.27 g, 1.34 mmol) in acetone (10 mL) was added 2,4-difluorobenzyl bromide (0.16 g, 0.8 mmol), and the reaction mixture was heated at reflux for 1 h. The reaction mixture was cooled to room temperature,
30 concentrated under reduced pressure, and the residue was dissolved in EtOAc. The organic solution was washed with water and then brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. ^1H NMR (300 MHz, CDCl_3) δ 7.65-7.55

(m, 1H), 7.40-7.25 (m, 2H), 7.15-6.80 (m, 5H), 6.14 (d, $J = 8$ Hz, 1H), 5.22 (s, 2H), 5.16 (s, 2H). ESHRMS m/z 424.0159 (M+H $C_{19}H_{14}BrF_3NO_2$ requires 424.0155).

5 Example 108

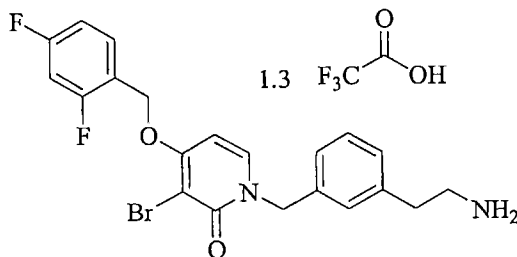


10 3-Bromo-1-(3-fluorobenzyl)-4-(2,3,4-trifluorobenzoyloxy)-1H-pyridin-2-one

The title compound was prepared by a procedure similar to the one described for Example 107 (0.09 g, 39%): mp 176-178 °C; 1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.25 (m, 4H), 7.11-6.98 (m, 4H), 6.11 (d, $J = 9$ Hz, 1H), 5.23 (s, 2H), 5.16 (s, 2H). ESHRMS m/z 442.0060 (M+H $C_{19}H_{13}BrF_4NO_2$ requires 442.0061)..

Example 109

20

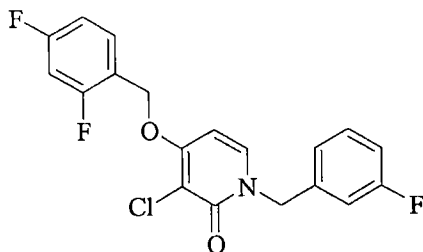


25 1-[3-(2-Aminoethyl)benzyl]-3-bromo-4-(2,4-difluorobenzoyloxy)-1H-pyridin-2-one

The title compound was prepared from compound of Example 97 by a procedure similar to the one described for Example 99, as the TFA salt (0.13 g, 33%): mp 70-74 °C; ¹H NMR (300 MHz, DMSO-
5 d₆) δ 8.21 (br s, 1H), 6.60-6.50 (m, 1H), 7.52 (d, J = 6 Hz, 1H), 7.30-7.10 (m, 3H), 7.01 (d, J = 9 Hz, 1H), 6.94-6.85 (m, 2H), 6.20 (d, J = 6 Hz, 1H), 5.20 (s, 2H), 5.05 (s, 2H), 3.23 (br s, 2H), 2.97 (t, J = 8 Hz, 2H), 2.05 (br s, 2H). ESHRMS m/z 449.0698 (M+H C₂₁H₂₀BrF₂N₂O₂ requires 449.0671).

10

Example 110



15

3-Chloro-4-(2,4-difluorobenzoyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one

Step 1. Preparation of 4-(2,4-difluorobenzoyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one.

20

To a solution of 1-(3-fluorobenzyl)-4-hydroxy-1H-pyridin-2-one (from Step 2 EXAMPLE 107) (0.92 g, 4.2 mmol) and K₂CO₃ (1.2 g, 8.4 mmol) in acetone (62 mL) was added 2,4-difluorobenzyl bromide (1.3 g, 6.3 mmol), and the reaction mixture was heated
25 at reflux for 3 h. The reaction mixture was cooled room temperature, concentrated under reduced pressure, and the residue was partitioned between water and EtOAc. The organic solution was washed with brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash

column chromatography (silica, eluent methylene chloride to 95:5 methylene chloride/methanol) to provide 4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one as a white solid (1.21 g, 84%): ^1H NMR (300 MHz, CDCl_3) δ 7.45-7.20 (m, 2H), 7.14 (d, J = 8 Hz, 1H), 7.05-6.75 (m, 5H), 6.05 (d, J = 3 Hz, 1H), 5.95 (dd, J = 5, 3 Hz, 1H), 5.08 (s, 2H), 5.00 (s, 2H).

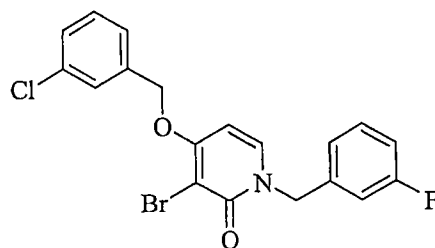
Step 2. Preparation of 3-Chloro-4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one.

To a solution of 4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one (0.15 g, 0.4 mmol) in AcOH (3 mL) was added N-chlorosuccinimide (70 mg, 0.5 mmol), and the reaction mixture was heated at reflux for 10 min. The reaction mixture was cooled room temperature and the solvent was removed under reduced pressure. ^1H NMR (300 MHz, CDCl_3) δ 7.60-7.50 (m, 1H), 7.45-7.20 (m, 2H), 7.10-6.80 (m, 5H), 6.16 (d, J = 8 Hz, 1H), 5.21 (s, 2H), 5.15 (s, 2H). ESHRMS m/z 380.0641 ($\text{M}+\text{H}$ $\text{C}_{19}\text{H}_{14}\text{ClF}_3\text{NO}_2$ requires 480.0660).

Examples 111-123

The following example compounds were prepared by procedures similar to that described for Example 107. The yields and the analytical data are described below.

Example 111

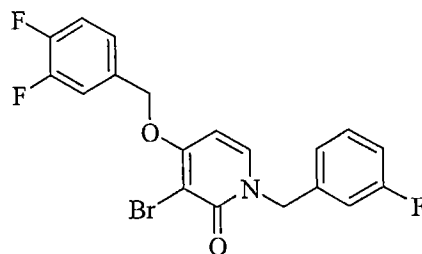


3-Bromo-4-(3-chlorobenzoyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one

5

The title compound was prepared by a procedure similar to the one described for EXAMPLE 107 (0.12 g, 42%): mp 149-153 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.23 (m, 6H), 7.09 (d, J = 8 Hz, 1H), 7.05-6.95 (m, 2H), 6.05 (d, J = 8 Hz, 1H), 5.19 (s, 2H),
 10 5.14 (s, 2H). ESMS m/z M+H 442.

Example 112



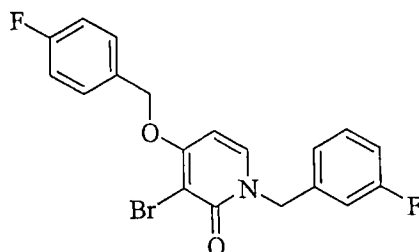
15

3-Bromo-4-(3,4-difluorobenzoyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one

20 The title compound was prepared by a procedure similar to the one described for EXAMPLE 107 (0.08 g, 48%): mp 172-174 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.40-6.95 (m, 8H), 6.05 (d, J = 6 Hz, 1H), 5.16 (s, 4H). ESHRMS m/z 424.0111 (M+H C₁₉H₁₄BrF₃NO₂ requires 424.0155).

25

Example 113

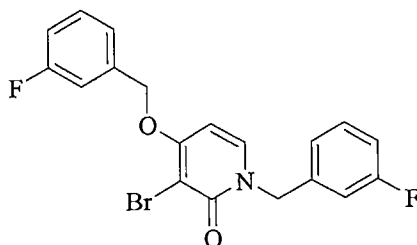


5

3-Bromo-1-(3-fluorobenzyl)-4-(4-fluorobenzyloxy)-1H-pyridin-2-one

The title compound was prepared by a procedure similar to the one described for EXAMPLE 107 (0.07 g, 35%): mp 180-183 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.50-7.25 (m, 5H), 7.15-7.00 (m, 4H), 6.07 (d, *J* = 8 Hz, 1H), 5.18 (s, 2H), 5.14 (s, 2H). ESHRMS *m/z* 406.0258 (M+H C₁₉H₁₅BrF₂NO₂ requires 406.0249).

15 Example 114



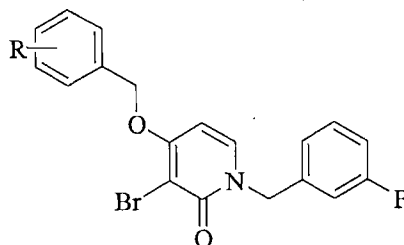
20 3-Bromo-1-(3-fluorobenzyl)-4-(3-fluorobenzyloxy)-1H-pyridin-2-one

To an ice-cold solution of 1-(3-fluorobenzyl)-4-(3-fluorobenzyloxy)-1H-pyridin-2-one (0.14 g, 0.43 mmol) in AcOH (2 mL) was added a solution of bromine (72 mg, 0.45 mmol) in

AcOH (1 mL), and the reaction mixture was stirred for 5 min. The reaction mixture was warmed to room temperature and the solvent was removed under reduced pressure. ^1H NMR (300 MHz, CDCl_3) δ 7.45-6.95 (m, 9H), 6.05 (d, J = 8 Hz, 1H), 5.21 (s, 2H), 5.14 (s, 2H). ESHRMS m/z 406.0254 ($\text{M}+\text{H}$ $\text{C}_{19}\text{H}_{15}\text{BrF}_2\text{NO}_2$ requires 406.0249).

Examples 115-123

The compounds of Examples 115-123 are prepared essentially according to the procedures set forth above for Example 107:



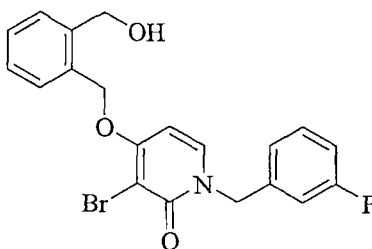
Example No.	R	MF	M+H Requires	ESHRMS m/z
Ex. 115	3-methoxy	$\text{C}_{20}\text{H}_{17}\text{BrFNO}_3$	418.0449	418.0427
Ex. 116	4-tert-butyl	$\text{C}_{23}\text{H}_{23}\text{BrFNO}_2$	444.0969	444.0977
Ex. 117	3-methyl	$\text{C}_{20}\text{H}_{17}\text{BrFNO}_2$	402.0499	402.0513
Ex. 118	4-trifluoromethyl	$\text{C}_{20}\text{H}_{14}\text{BrF}_4\text{NO}_2$	456.0217	456.0210
Ex. 119	4-cyano	$\text{C}_{20}\text{H}_{14}\text{BrFN}_2\text{O}_2$	413.0295	413.0313
Ex. 120	2-methyl	$\text{C}_{20}\text{H}_{17}\text{BrFNO}_2$	402.0499	402.0502
Ex. 121	2-phenyl	$\text{C}_{25}\text{H}_{19}\text{BrFNO}_2$	464.0656	464.0654
Ex. 122	4-methoxy	$\text{C}_{20}\text{H}_{17}\text{BrFNO}_3$	418.0449	418.0455
Ex. 123	2-CO ₂ CH ₃	$\text{C}_{21}\text{H}_{17}\text{BrFNO}_4$	446.0398	446.0403

NMR characterization of compounds of Examples 115-123

Example	NMR Data
---------	----------

No.	
Ex. 115	¹ H NMR (300 MHz, CDCl ₃) δ 7.35-7.20 (m, 4H), 7.15-6.85 (m, 5H), 6.07 (d, J = 8 Hz, 1H), 5.21 (s, 2H), 5.13 (s, 2H), 3.82 (s, 3H)
Ex. 116	¹ H NMR (300 MHz, CDCl ₃) δ 7.45-7.20 (m, 4H), 7.10-6.95 (m, 3H), 6.11 (d, J = 8 Hz, 1H), 5.19 (s, 2H), 5.14 (s, 2H), 1.32 (s, 9H)
Ex. 117	¹ H NMR (300 MHz, CDCl ₃) δ 7.40-6.90 (m, 9H), 6.08 (d, J = 8 Hz, 1H), 5.19 (s, 2H), 5.14 (s, 2H), 2.37 (s, 3H)
Ex. 118	¹ H NMR (300 MHz, CDCl ₃) δ 7.67-7.53 (m, 4H), 7.31-7.24 (m, 2H), 7.09-6.98 (m, 3H), 6.04 (d, J = 8 Hz, 1H), 5.26 (s, 2H), 5.14 (s, 2H)
Ex. 119	¹ H NMR (300 MHz, CDCl ₃) δ 7.71 (dd, J = 8, 2 Hz, 2H), 7.58-7.55 (m, 2H), 7.29-7.25 (m, 2H), 7.09 (d, J = 8 Hz, 1H), 7.03-6.98 (m, 2H), 6.03 (dd, J = 8, 2 Hz, 1H), 5.26 (s, 2H), 5.15 (s, 2H)
Ex. 120	¹ H NMR (300 MHz, CDCl ₃) δ 7.45-6.90 (m, 9H), 6.15-6.10 (m, 1H), 5.18 (s, 2H), 5.15 (s, 2H), 2.38 (s, 3H)
Ex. 121	¹ H NMR (300 MHz, CDCl ₃) δ 7.70-7.65 (m, 1H), 7.55-7.25 (m, 9H), 7.14 (d, J = 8 Hz, 1H), 7.10-6.95 (m, 3H), 5.81 (d, J = 8 Hz, 1H), 5.12 (s, 2H), 5.08 (s, 2H)
Ex. 122	¹ H NMR (300 MHz, CDCl ₃) δ 7.40-7.25 (m, 3H), 7.15-6.90 (m, 6H), 6.15-6.10 (m, 1H), 5.16 (s, 2H), 5.14 (s, 2H), 3.82 (s, 3H)
Ex. 123	¹ H NMR (300 MHz, CDCl ₃) δ 8.06 (dd, J = 8, 1 Hz, 1H), 7.87 (d, J = 8 Hz, 1H), 7.70-7.60 (m, 1H), 7.50-7.25 (m, 3H), 7.09 (d, J = 8 Hz, 1H), 7.05-6.95 (m, 2H), 6.19 (d, J = 8 Hz, 1H), 5.65 (s, 2H), 5.16 (s, 2H), 3.91 (s, 3H)

Example 124



5

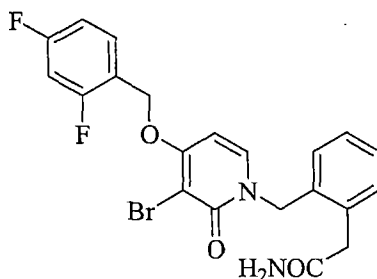
3-Bromo-1-(3-fluorobenzyl)-4-(2-hydroxymethylbenzyloxy)-1H-pyridin-2-one

10 Step 1. Preparation of 3-Bromo-1-(3-fluorobenzyl)-4-(2-hydroxymethylbenzyloxy)-1H-pyridin-2-one.

To an ice-cold solution of methyl 2-[3-bromo-1-(3-fluorobenzyl)-2-oxo-1,2-dihydro-pyridin-4-ylloxymethyl]benzoate

(0.12 g, 0.28 mmol) in THF (5 mL) was added LiBH₄ (0.15 mL of a 2.0 M solution in THF, 0.30 mmol), and the reaction mixture heated at reflux for 5 hours. The reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure, and the residue dissolved in EtOAc. The organic solution was washed with brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.98 (d, *J* = 8 Hz, 1H), 7.46-7.28 (m, 5H), 7.15-7.10 (m, 3H), 6.56 (d, *J* = 8 Hz, 1H), 5.35 (s, 2H), 5.25 (br s, 1H), 5.14 (s, 2H). ESHRMS *m/z* 418.0453 (M+H C₂₀H₁₈BrFNO₃ requires 418.0449).

Example 126



2-{2-[3-Bromo-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]-phenyl}acetamide

Step 1. Preparation of (2-Bromomethylphenyl)acetic acid.

A solution of isochroman-3-one (1.5 g, 10 mmol) in 30% HBr in acetic acid (13 mL) was stirred at room temperature for 2 h, and 70 °C for 1 h. The reaction mixture was cooled to room temperature, and poured into ice-water. The precipitate was collected to afford (2-bromomethylphenyl)acetic acid as an off-white solid (2.15 g, 93%): ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.45-7.23 (m, 4H), 4.73 (s, 2H), 3.73 (s, 2H).

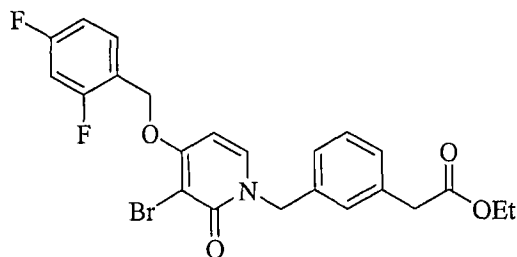
Step 2. Preparation of Methyl (2-Bromomethylphenyl)acetate.

To an ice-cold solution of (2-bromomethylphenyl)acetic acid (1 g, 4.4 mmol) in THF (2.4 mL) was added trimethylsilyldiazomethane (3 mL of a 2 M solution in hexanes, 6 mmol), and the reaction mixture was stirred for 14 h. The reaction was quenched with AcOH, and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica, eluent 98:2 to 94:6 methylene chloride/hexanes) afforded methyl (2-bromomethylphenyl)acetate as a light yellow solid (0.34 g, 32%): ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.20 (m, 4H), 4.59 (s, 2H), 3.81 (s, 2H), 3.71 (s, 3H).

Step 3. Preparation of Methyl {2-[3-bromo-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]phenyl}acetate. Methyl {2-[3-bromo-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]phenyl}acetate was prepared by a procedure similar to the one described for EXAMPLE 74 (0.41 g, 68%): ^1H NMR (300 MHz, CDCl_3) δ 7.55-6.81 (m, 8 H), 6.10 (d, J = 6 Hz, 1H), 5.20 (s, 4 H), 3.78 (s, 2H), 3.60 (s, 3H).

Step 4. Preparation of 2-{2-[3-Bromo-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]phenyl}acetamide. 2-{2-[3-Bromo-4-(2,4-difluorobenzyloxy)-2-oxo-2H-pyridin-1-ylmethyl]phenyl}-acetamide was prepared by a procedure similar to the one described for Example 102 (0.07 g, 72%): mp 178-183 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.89 (d, J = 8 Hz, 1H), 7.66 (d, J = 9 Hz, 1 H), 7.54 (br s, 1H), 7.35 (br s, 1H), 7.30-7.15 (m, 4H), 6.98 (br s, 1H), 6.85 (d, J = 7 Hz, 1H), 6.60 (d, J = 8 Hz, 1H), 5.32 (s, 2H), 5.19 (s, 2H), 3.62 (s, 2H). ESHRMS m/z 463.0442 ($M+H$ $\text{C}_{21}\text{H}_{18}\text{BrF}_2\text{N}_2\text{O}_3$ requires 463.0463).

Example 127



5 Ethyl {3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-
1-ylmethyl]-phenyl}acetate

Step 1. Preparation of Ethyl (3-bromomethylphenyl) acetate.

To a mixture of *m*-tolylacetic acid ethyl ester (3.0 g, 16.8
10 mmol) and N-bromosuccinimide (3.0 g, 16.8 mmol) was added
carbon tetrachloride (45 mL), followed by benzoyl peroxide (5
mg), and the reaction mixture was heated at reflux for 16 h.
The reaction mixture was cooled to room temperature, filtered,
and concentrated under reduced pressure. Purification by
15 flash column chromatography (silica, eluent 5:95 to 2:3
EtOAc/hexanes) afforded ethyl (3-bromomethylphenyl) acetate as
an off-white solid (0.89 g, 21%): ¹H NMR (300 MHz, CDCl₃) δ
7.32-7.21 (m, 4H), 4.48 (s, 2H), 4.16 (q, *J* = 6 Hz, 2H), 3.63,
(s, 2H), 1.27 (t, *J* = 6 Hz, 3H).

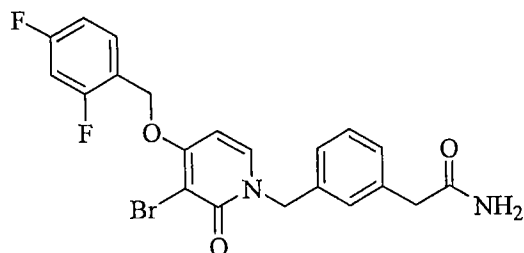
20

Step 2. Preparation of Ethyl {3-[3-Bromo-4-(2,4-
difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl]phenyl}acetate.
Ethyl {3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-
1-ylmethyl]phenyl}-acetate was prepared by a procedure similar
25 to the one described for EXAMPLE 74 (0.27 g, 69%): mp 95-98
°C; ¹H NMR (300 MHz, CDCl₃) δ 7.65-7.55 (m, 1H), 7.40-7.20 (m,
5H), 7.00-6.80 (m, 2H), 6.09 (d, *J* = 9 Hz, 1H), 5.21 (s, 2H),
5.16 (s, 2H), 4.14 (q, *J* = 6 Hz, 2H), 3.60 (s, 2H), 1.25 (t, *J*

= 6 Hz, 3H). ESHRMS m/z 492.0655 ($M+H$ $C_{23}H_{21}BrF_2NO_4$ requires 435.0617).

Example 128

5



10

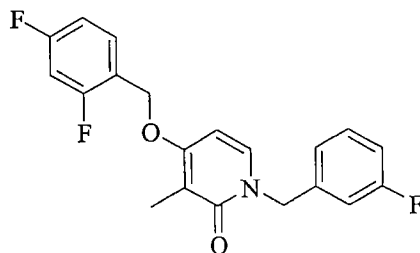
2-{3-[3-Bromo-4-(2,4-difluorobenzoyloxy)-2-oxo-2H-pyridin-1-ylmethyl] phenyl} acetamide

15

The title compound was prepared by a procedure similar to the one described for EXAMPLE 102 (0.07 g, 28%): mp 164-167 °C; 1H NMR (300 MHz, $DMSO-d_6$) δ 7.96 (d, J = 9 Hz, 1H), 7.70-7.60 (m, 1H), 7.60 (br s, 1H), 7.50-7.10 (m, 6H), 6.89 (br s, 1H), 6.58 (d, J = 9 Hz, 1H), 5.31 (s, 2H), 5.12 (s, 2H), 3.32 (s, 2H). ESHRMS m/z 463.0485 ($M+H$ $C_{21}H_{18}BrF_2N_2O_3$ requires 463.0464).

Example 129

20



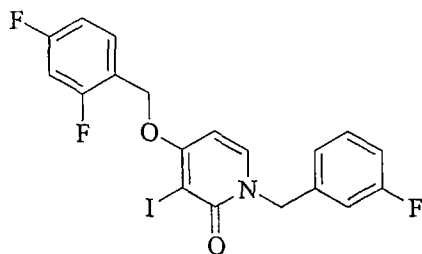
4-(2,4-Difluorobenzoyloxy)-1-(3-fluorobenzyl)-3-methyl-1H-pyridin-2-one

25

Step 1. Preparation of 4-(2,4-Difluorobenzoyloxy)-1-(3-fluorobenzyl)-3-methyl-1H-pyridin-2-one.

To a solution of 3-bromo-4-(2,4-difluorobenzoyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one (EXAMPLE 107) (0.14 g, 0.32 mmol), K₂CO₃ (88 mg, 0.64 mmol) and Cs₂CO₃ (0.10 g, 0.32 mmol) in dioxane (2 mL) was added Pd(PPh₃)₄ (18 mg, 0.12 mmol), followed by trimethylboroxine (40 mg, 0.32 mmol). The reaction mixture was degassed, purged with argon, and heated at reflux for 4 h. The reaction mixture was cooled to room temperature, and partitioned between water and EtOAc. The organic solution was washed with brine, dried (Na₂SO₄), filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica, eluent methylene chloride to 97:3 methylene chloride/MeOH) afforded 4-(2,4-difluorobenzoyloxy)-1-(3-fluorobenzyl)-3-methyl-1H-pyridin-2-one as a white solid (0.09 g, 79%): mp 127-129 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.50-7.40 (m, 1H), 7.35-7.25 (m, 1H), 7.17 (d, J = 9 Hz, 1H), 7.06 (d, J = 6 Hz, 1H), 7.00-6.80 (m, 4H), 6.12 (d, J = 9 Hz, 1H), 5.12 (s, 4H), 2.07 (s, 3H). ESHRMS m/z 360.1180 (M+H C₂₀H₁₆F₃NO₂ requires 360.1206).

Example 130



4-(2,4-Difluorobenzoyloxy)-1-(3-fluorobenzyl)-3-iodo-1H-pyridin-2-one

Step 1. Preparation of 4-(2,4-Difluorobenzoyloxy)-1-(3-fluorobenzyl)-1H-pyridin-2-one.

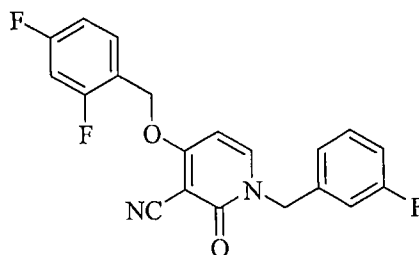
To a mixture of 1-(3-fluorobenzyl)-4-hydroxy-1*H*-pyridin-2-one (from Step 1, EXAMPLE 110) (0.92 g, 4.2 mmol) and K₂CO₃ (1.15 g, 8.4 mmol) in acetone (62 mL) was added 2,4-difluorobenzyl bromide (1.3 g, 6.3 mmol), and the reaction mixture was heated
5 at reflux for 3 h. The reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the residue was dissolved in EtOAc. The organic solution was washed with water and then brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash
10 column chromatography (silica, eluent methylene chloride to 95:5 methylene chloride/methanol) provided 4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-1*H*-pyridin-2-one as a white solid (1.21 g, 84%): ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.20 (m, 2H), 7.14 (d, *J* = 8 Hz, 1H), 7.05-6.75 (m, 5H), 6.05 (d, *J* = 3 Hz, 1H), 5.95 (dd, *J* = 5, 3 Hz, 1H), 5.08 (s, 2H), 5.00 (s, 2H).

Step 2. Preparation of 4-(2,4-Difluorobenzyloxy)-1-(3-fluorobenzyl)-3-iodo-1*H*-pyridin-2-one.

20 To a mixture of 4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-1*H*-pyridin-2-one (0.15 g, 0.43 mmol) and N-iodosuccinimide (0.10 g, 0.46 mmol) in CH₃CN (3 mL) was added dichloroacetic acid (13 mg, 0.10 mmol), and the reaction mixture was heated to 60 °C for 4 h. The reaction mixture was cooled to room
25 temperature, concentrated under reduced pressure, and the residue was dissolved in methylene chloride. The organic solution was washed with a saturated solution of NaHCO₃ and then brine, dried (Na₂SO₄), filtered and concentrated under reduced pressure. Purification by flash column chromatography
30 (silica, eluent 90:10 methylene chloride/hexanes to 99:1 methylene chloride/methanol) provided 4-(2,4-difluorobenzyloxy)-1-(3-fluorobenzyl)-3-iodo-1*H*-pyridin-2-one as a white solid (0.15 g, 77%): mp 164-167 °C; ¹H NMR (300 MHz,

CDCl₃) δ 7.65-7.55 (m, 1H), 7.35-7.26 (m, 2H) 7.15-6.80 (m, 5H), 6.05 (d, J = 6 Hz, 1H), 5.22 (s, 2H), 5.16 (s, 2H).
 ESHRMS m/z 472.0033 (M+H C₁₉H₁₄F₃INO₂ requires 472.0018).

5 Example 131



4-(2,4-Difluorobenzyloxy)-1-(3-fluorobenzyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile

10

Step 1. Preparation of 4-Methoxy-2-oxo-1,2-dihydropyridine-3-carbonitrile.

A solution of 2-(dimethylaminoethoxymethylene)malononitrile (1.97 g) in concentrated sulfuric acid (7.0 mL) was stirred at
 15 room temperature for 6.5 h. The reaction mixture was poured into water, and the precipitate was collected by filtration.
¹H NMR (300 MHz, DMSO-*d*₆) δ 12.14 (br s, 1H), 7.79 (d, J = 9 Hz, 1H), 6.35 (d, J = 9 Hz, 1H), 3.98 (s, 3H).

20 Step 2. Preparation of 1-(3-Fluorobenzyl)-4-methoxy-2-oxo-1,2-dihydro-pyridine-3-carbonitrile.

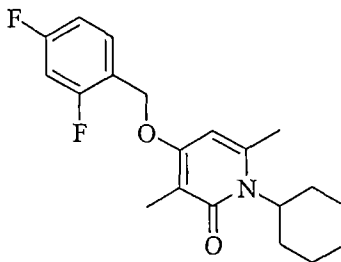
1-(3-Fluorobenzyl)-4-methoxy-2-oxo-1,2-dihydro-pyridine-3-carbonitrile was prepared by a procedure similar to the one described for EXAMPLE 74 (0.56 g, 93%): ¹H NMR (300 MHz, CDCl₃)
 25 δ 7.48 (d, J = 9 Hz, 1H), 7.40-7.27 (m, 1H), 7.00-6.95 (m, 2H), 6.08 (d, J = 9 Hz, 1H), 5.10 (s, 2H), 4.00 (s, 3H).

Step 3. Preparation of 1-(3-Fluorobenzyl)-4-hydroxy-2-oxo-1,2-dihydropyridine-3-carbonitrile.

To a solution of sodium hydride (92 mg of a 60% dispersion in mineral oil, 2.3 mmol) in DMF (7 mL) was added ethanethiol (0.14 g, 2.2 mmol), followed by a solution of 1-(3-fluorobenzyl)-4-methoxy-2-oxo-1,2-dihydropyridine-3-carbonitrile (0.23 g, 0.89 mmol) in DMF (2 mL), and the reaction mixture was heated to 100 °C. The reaction mixture was cooled to room temperature, acidified with 3 N HCl, and washed with EtOAc. The organic solution was washed with brine, dried (Na₂SO₄), filtered and concentrated under reduced pressure to give 1-(3-fluorobenzyl)-4-hydroxy-2-oxo-1,2-dihydro-pyridine-3-carbonitrile as an off-white solid (0.20 g, 91%): ¹H NMR (300 MHz, MeOD) δ 8.00 (s, 1H), 7.82 (d, J = 8 Hz, 1H), 7.40-7.30 (m, 1H), 7.15-7.00 (m, 2H), 6.13 (d, J = 8 Hz, 1H), 5.11 (s, 2H).

Step 4. Preparation of 4-(2,4-Difluorobenzoyloxy)-1-(3-fluorobenzyl)-2-oxo-1,2-dihydro-pyridine-3-carbonitrile. 4-(2,4-Difluorobenzoyloxy)-1-(3-fluorobenzyl)-2-oxo-1,2-dihydro-pyridine-3-carbonitrile was prepared by a procedure similar to the one described for EXAMPLE 107 (0.09 g, 30%): mp 187-190 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.60-7.45 (m, 2H), 7.40-7.30 (m, 1H), 7.10-6.50 (m, 5H), 6.13 (d, J = 9 Hz, 1H), 5.27 (s, 2H), 5.10 (s, 2H).

Example 132



1-Cyclohexyl-4-(2,4-difluorobenzyloxy)-3,6-dimethyl-1H-
pyridin-2-one

Step 1. Preparation of Methyl 1-cyclohexyl-4-hydroxy-2,5-
5 dimethyl-6-oxo-1,6-dihydro-pyridine-3-carboxylate.

To a solution of 3-cyclohexylaminobut-2-enoic acid methyl
ester (1.12 g, 5.72 mmol) in bromobenzene (20 mL) was added 2-
methylmalonic acid bis-(2,4,6-trichloro-phenyl) ester (2.71 g,
5.72 mmol) and the reaction mixture was heated at 170 °C for 3

10 h. The reaction mixture was cooled to room temperature, and
concentrated under reduced pressure. Purification by flash
column chromatography (silica, eluent methylene chloride to
94:6 methylene chloride/MeOH) and recrystallization from hot
MeOH provided methyl 1-cyclohexyl-4-hydroxy-2,5-dimethyl-6-
15 oxo-1,6-dihydropyridine-3-carboxylate as pale yellow crystals
(0.34 g, 21%): ¹H NMR (500 MHz, DMSO-d₆) δ 9.82 (s, 1H), 4.00-
3.90 (m, 1H), 3.76 (s, 3H), 2.75-2.60 (m, 2H), 2.31 (s, 3H),
1.81 (s, 3H), 1.80-1.70 (m, 2H), 1.65-1.50 (m, 3H), 1.40-1.20
(m, 2H), 1.15-1.05 (m, 1H).

20 Step 2. Preparation of 1-Cyclohexyl-4-hydroxy-2,5-dimethyl-6-
oxo-1,6-dihydro-pyridine-3-carboxylic acid.

A solution of methyl 1-cyclohexyl-4-hydroxy-2,5-dimethyl-6-
oxo-1,6-dihydro-pyridine-3-carboxylate (0.35 g, 1.25 mmol) in
25 2 N NaOH (5 mL) was heated at reflux for 3.5 h. The reaction
mixture was cooled room temperature, acidified to pH 1-2 with
1 N HCl, and washed with EtOAc. The organic solution was
washed with brine, dried (MgSO₄), filtered and concentrated
under reduced pressure to afford 1-cyclohexyl-4-hydroxy-2,5-
30 dimethyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid as a
white solid (0.31 g, 94%): ¹H NMR (300 MHz, MeOD) δ 4.30-4.00
(br s, 1H), 2.76 (br s, 5H), 1.90 (s, 3H), 1.90-1.80 (m, 2H),
1.75-1.60 (m, 3 H), 1.50-1.15 (m, 3H).

Step 3. Preparation of 1-Cyclohexyl-4-hydroxy-3,6-dimethyl-1H-pyridin-2-one.

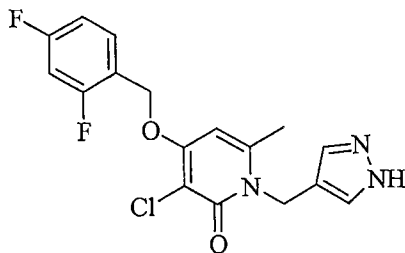
A solution of 1-cyclohexyl-4-hydroxy-2,5-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid (0.15 g, 0.57 mmol) in concentrated HCl (5 mL) was heated at reflux for 4 h. The reaction mixture was cooled to room temperature, diluted with water and washed with EtOAc. The organic solution was washed with brine, dried (MgSO₄), filtered and concentrated under reduced pressure to give 1-cyclohexyl-4-hydroxy-3,6-dimethyl-1H-pyridin-2-one as a white solid (0.2 g, 77%): ¹H NMR (300 MHz, DMSO-d₆) δ 9.81 (s, 1H), 5.73 (s, 1H), 3.95-3.75 (m, 1H), 2.80-2.55 (m, 2H), 2.25 (s, 3H), 1.85-1.40 (m, 5H), 1.72 (s, 3H), 1.38-1.05 (m, 3H).

Step 4. Preparation of 1-Cyclohexyl-4-(2,4-difluorobenzoyloxy)-3,6-dimethyl-1H-pyridin-2-one.

1-Cyclohexyl-4-(2,4-difluorobenzoyloxy)-3,6-dimethyl-1H-pyridin-2-one was prepared by a procedure similar to the one

described for EXAMPLE 107 (0.05 g, 16%): mp 118-120 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.48-7.41 (m, 1H), 6.95-6.81 (m, 2H), 5.87 (s, 1H), 5.07 (s, 2H), 4.05-3.85 (m, 1H), 3.00-2.80 (m, 2H), 2.35 (s, 3H), 1.98 (s, 3H), 1.95-1.80 (m, 2H), 1.70-1.55 (m, 3H), 1.40-1.20 (m, 3H).

Example 133



3-Chloro-4-(2,4-difluorobenzyloxy)-6-methyl-1-(1H-pyrazol-4-ylmethyl)-1H-pyridin-2-one

Step 1. Preparation of 4-Methylpyrazole-1-carboxylic acid
5 tert-butyl ester.

To a solution of 4-methyl-1H-pyrazole (1 g, 12 mmol) and DMAP (0.15 g, 1.2 mmol) in CH₃CN (20 mL) was added di-tert-butyl dicarbonate (2.8 g, 13 mmol), and the reaction mixture was stirred for 1 h. The reaction mixture was concentrated under
10 reduced pressure, and the residue dissolved in EtOAc. The organic solution was washed with 1 N HCl, water and then brine, dried (MgSO₄), filtered, and concentrated under reduced pressure to provide 4-methyl-pyrazole-1-carboxylic acid tert-butyl ester as a light yellow oil (2.2 g, 100%): ¹H NMR (300
15 MHz, CDCl₃) δ 7.83 (s, 1H), 7.53 (s, 1H), 2.09 (s, 3H), 1.64 (s, 9H).

Step 2. Preparation of 4-Bromomethylpyrazole-1-carboxylic acid tert-butyl ester.

20 To a solution of 4-methylpyrazole-1-carboxylic acid tert-butyl ester (1.0 g, 5.5 mmol) in carbon tetrachloride (20 mL) was added N-bromosuccinimide (1.0 g, 5.6 mmol) and benzoyl peroxide (50 mg), and the reaction mixture was heated at reflux for 16 h. The reaction mixture was cooled to room
25 temperature, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:4 EtOAc/hexanes) provided 4-bromomethylpyrazole-1-carboxylic acid tert-butyl ester as a light yellow oil (0.42 g, 30%): ¹H NMR (300 MHz, CDCl₃) δ 8.10 (s, 1H), 7.74 (s, 1H),
30 4.39 (s, 2H), 1.65 (s, 9H).

Step 3. Preparation of 4-[3-Chloro-4-(2,4-difluorobenzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]pyrazole-1-carboxylic acid *tert*-butyl ester.

4-[3-Chloro-4-(2,4-difluorobenzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]pyrazole-1-carboxylic acid *tert*-butyl ester was prepared by a procedure similar to the one described for EXAMPLE 632: ^1H NMR (300 MHz, CDCl_3) δ 8.09 (s, 1H), 7.72 (s, 1H), 7.53 (app q, $J = 6$ Hz, 1H), 6.97-6.82 (m, 2H), 6.00 (s, 1H), 5.19 (s, 2H), 5.13 (s, 2H), 2.43 (s, 3H), 1.63 (s, 9H).

Step 4. Preparation of 3-Chloro-4-(2,4-difluorobenzyloxy)-6-methyl-1-(1H-pyrazol-4-ylmethyl)-1H-pyridin-2-one.

4-[3-Chloro-4-(2,4-difluorobenzyloxy)-6-methyl-2-oxo-2H-pyridin-1-ylmethyl]pyrazole-1-carboxylic acid *tert*-butyl ester (0.16 g, 0.34 mmol) was heated to 140 °C for 16 h. The reaction mixture was cooled to room temperature. ^1H NMR (300 MHz, CDCl_3) δ 8.33 (s, 2H), 7.68 (d, $J = 6$ Hz, 1H), 7.52 (app q, $J = 6$ Hz, 1H), 6.93-6.83 (m, 2H), 6.47-6.38 (d, $J = 9$ Hz, 1H), 5.19 (s, 2H), 5.24 (s, 2H), 5.20 (s, 2H).

Example 134

4-{[4-(benzyloxy)-3-bromo-2-oxopyridin-1(2H)-yl]methyl}benzonitrile

